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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

#### (57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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# COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

#### TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

#### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of canoer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polypucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T-cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preserably mRNA, that hybridizes to the oligonucleotide and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic

kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

# BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13 SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-186
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-186
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
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SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864 SEQ ID NO: 41 is the determined cDNA sequence for P5 SEQ ID NO: 42 is the determined cDNA sequence for P8 SEQ ID NO: 43 is the determined cDNA sequence for P9 SEQ ID NO: 44 is the determined cDNA sequence for P18 SEQ ID NO: 45 is the determined cDNA sequence for P20 SEQ ID NO: 46 is the determined cDNA sequence for P29 SEQ ID NO: 47 is the determined cDNA sequence for P30 SEQ ID NO: 48 is the determined cDNA sequence for P34 SEQ ID NO: 49 is the determined cDNA sequence for P36 SEQ ID NO: 50 is the determined cDNA sequence for P38 SEQ ID NO: 51 is the determined cDNA sequence for P39 SEQ ID NO: 52 is the determined cDNA sequence for P42 SEQ ID NO: 53 is the determined cDNA sequence for P47 SEQ ID NO: 54 is the determined cDNA sequence for P49 SEQ ID NO: 55 is the determined cDNA sequence for P50 SEQ ID NO: 56 is the determined cDNA sequence for P53 SEQ ID NO: 57 is the determined cDNA sequence for P55 SEQ ID NO: 58 is the determined cDNA sequence for P60 SEQ ID NO: 59 is the determined cDNA sequence for P64 SEQ ID NO: 60 is the determined cDNA sequence for P65 SEQ ID NO: 61 is the determined cDNA sequence for P73 SEQ ID NO: 62 is the determined cDNA sequence for P75 SEQ ID NO: 63 is the determined cDNA sequence for P76 SEQ ID NO: 64 is the determined cDNA sequence for P79 SEQ ID NO: 65 is the determined cDNA sequence for P84 SEQ ID NO: 66 is the determined cDNA sequence for P68 SEQ ID NO: 67 is the determined cDNA sequence for P80 SEQ ID NO: 68 is the determined cDNA sequence for P82 SEQ ID NO: 69 is the determined cDNA sequence for U1-3064 SEQ ID NO: 70 is the determined cDNA sequence for U1-3065 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692 SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905 SEQ ID NO: 73 is the determined cDNA sequence for V1-3686 SEQ ID NO: 74 is the determined cDNA sequence for R1-2330 SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ 10 NO. 77 is the determined CDNA sequence for 10-4736	
SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738	•
SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741	
SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744	
SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734	
SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774	•
SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781	•
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SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787	
SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796	
SEQ ID NO: 87 is the determined cDNA sequence for 11-4807	. •
SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810	
SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811	
SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876	
SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884	
SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896	•
SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761	
SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762	
SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766	
SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770	(()
SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771	
SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772	
SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297	
SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309	* 0
SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278	-
SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288	
SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283	*
SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304	
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296	- (*)
SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280	
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (als	so referred to as
P504S)	
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12	
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17	
SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12	
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862	
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17	· · · · · · · · · · · · · · · · · · ·

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12
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SEQ ID NO: 124 is the determined cDNA sequence for P115
SEQ ID NO: 125 is the determined cDNA sequence for P116
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SEQ ID NO: 127 is the determined cDNA sequence for P126
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SEQ ID NO: 130 is the determined cDNA sequence for P138
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SEQ ID NO: 133 is the determined cDNA sequence for P156
SEQ ID NO: 134 is the determined cDNA sequence for P157
SEQ ID NO: 135 is the determined cDNA sequence for P166
SEQ ID NO: 136 is the determined cDNA sequence for P176
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SEQ ID NO: 138 is the determined cDNA sequence for P179
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SEQ ID NO: 147 is the determined cDNA sequence for P237
SEQ ID NO: 148 is the determined cDNA sequence for P239
SEO ID NO: 140 is the determined mDNA converse for D249

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SEQ ID NO: 163 is the determined cDNA sequence for P137
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SEQ ID NO: 165 is the determined cDNA sequence for P195
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SEQ ID NO: 167 is the determined cDNA sequence for P220
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SEQ ID NO: 170 is the determined cDNA sequence for P243
SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13
SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14
SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14
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SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785
SEO ID NO: 186 is the determined extended cDNA sequence for 1H-4782

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-4796 SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-4807 SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876 SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884 SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896 SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766 SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770 SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771 SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772 SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288 SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283 SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304 SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd SEQ ID NO: 211 is the determined cDNA sequence for 7-g6rev SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S
SEQ ID NO: 225 is the determined cDNA sequence for P703DE
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN1
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN1
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN2
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN2:
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

100 100 100 101 is the determined CDIAA sequence for 31 1D3
SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

SEQ ID NO: 298 is the determined cDNA sequence for JP8C10 SEQ ID NO: 299 is the determined cDNA sequence for JP8E9 SEQ ID NO: 300 is the determined cDNA sequence for JP8E10 SEQ ID NO: 301 is the determined cDNA sequence for JP8F9 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12 SEQ ID NO: 304 is the determined cDNA sequence for JP8E11 SEQ ID NO: 305 is the determined cDNA sequence for JP8E12 SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12 SEQ ID NO: 307 is the determined cDNA sequence for P711P SEQ ID NO: 308 is the determined cDNA sequence for P712P SEQ ID NO: 309 is the determined cDNA sequence for CLONE23 SEQ ID NO: 310 is the determined cDNA sequence for P774P SEQ ID NO: 311 is the determined cDNA sequence for P775P SEQ ID NO: 312 is the determined cDNA sequence for P715P SEQ ID NO: 313 is the determined cDNA sequence for P710P SEQ ID NO: 314 is the determined cDNA sequence for P767P SEQ ID NO: 315 is the determined cDNA sequence for P768P SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5 SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26 SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23 SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9) SEQ ID NO: 334 is the determined cDNA sequence for P714P SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3) SEQ ID NO: 336 is the predicted amino acid sequence for P705P SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10 SEQ ID NO: 338 is the amino acid sequence of the peptide p5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S SEQ ID NO: 340 is the determined cDNA sequence for P778P SEQ ID NO: 341 is the determined cDNA sequence for P786P SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO:389 is the cDNA sequence for 23379.

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571. SEQ ID NO:415 is the cDNA sequence for 22572. SEQ ID NO:416 is the cDNA sequence for 22573. SEQ ID NO:417 is the cDNA sequence for 22573. SEQ ID NO:418 is the cDNA sequence for 22575. SEQ ID NO:419 is the cDNA sequence for 22580. SEQ ID NO:420 is the cDNA sequence for 22581. SEQ ID NO:421 is the cDNA sequence for 22582. SEQ ID NO:422 is the cDNA sequence for 22583. SEQ ID NO:423 is the cDNA sequence for 22584. SEQ ID NO:424 is the cDNA sequence for 22585. SEQ ID NO:425 is the cDNA sequence for 22586. SEQ ID NO:426 is the cDNA sequence for 22587. SEQ ID NO:427 is the cDNA sequence for 22588. SEQ ID NO:428 is the cDNA sequence for 22589. SEQ ID NO:429 is the cDNA sequence for 22590. SEQ ID NO:430 is the cDNA sequence for 22591. SEQ ID NO:431 is the cDNA sequence for 22592. SEQ ID NO:432 is the cDNA sequence for 22593. SEQ ID NO:433 is the cDNA sequence for 22594. SEQ ID NO:434 is the cDNA sequence for 22595. SEQ ID NO:435 is the cDNA sequence for 22596. SEQ ID NO:436 is the cDNA sequence for 22847. SEQ ID NO:437 is the cDNA sequence for 22848. SEQ ID NO:438 is the cDNA sequence for 22849. SEQ ID NO:439 is the cDNA sequence for 22851. SEQ ID NO:440 is the cDNA sequence for 22852. SEQ ID NO:441 is the cDNA sequence for 22853. SEQ ID NO:442 is the cDNA sequence for 22854. SEQ ID NO:443 is the cDNA sequence for 22855. SEQ ID NO:444 is the cDNA sequence for 22856. SEQ ID NO:445 is the cDNA sequence for 22857. SEQ ID NO:446 is the cDNA sequence for 23601. SEQ ID NO:447 is the cDNA sequence for 23602. SEQ ID NO:448 is the cDNA sequence for 23605. SEQ ID NO:449 is the cDNA sequence for 23606. SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NOs:462-467 are cDNA sequences for known genes.

SEQ ID NOs:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

# DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

#### PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50,

in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e., gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e., the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to

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the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., Proc. Natl. Acad. Sci. USA 93:10614-10619, 1996 and Heller et al., Proc. Natl. Acad. Sci. USA 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with <sup>32</sup>P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using

standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these

polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability in vivo. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such

as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors.. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (i.e., an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

#### PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from

the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (i.e., specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, 123I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein.

Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are

E. coli, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into

the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from Streptococcus pneumoniae, which synthesizes an N-acetyl-L-alanine amidase known as

amidase LYTA (encoded by the LytA gene; Gene 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of E. coli C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

## **BINDING AGENTS**

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10<sup>3</sup> L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from

patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, Eur. J. Immunol. 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient

time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, Antibodies: A Laboratory Manual. Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include <sup>90</sup>Y, <sup>123</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>186</sup>Re, <sup>188</sup>Re, <sup>211</sup>At, and <sup>212</sup>Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and

thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATETM system, available from CellPro Inc., Bothell WA (*see also* U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience

(Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4 and/or CD8. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4+ or CD8+ T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either in vitro or in vivo. Proliferation of such T cells in vitro may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

# PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides. T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (i.e., vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated in situ. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, Crit. Rev. Therap. Drug Carrier Systems 15:143-198, 1998,

and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or

preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is

quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (i.e., a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects per se and/or to be immunologically compatible with the receiver (i.e., matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, Nature 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate in situ, with marked cytoplasmic processes (dendrites) visible in vitro) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be-engineered to express specific cell-

surface receptors or ligands that are not commonly found on dendritic cells in vivo or ex vivo, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., Nature Med. 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that

provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

### **CANCER THERAPY**

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8+ cytotoxic T lymphocytes and CD4+ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth in vitro, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition in vivo are well known in the art. Such in vitro culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein

may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated ex vivo for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such

a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding

agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20<sup>TM</sup> (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20<sup>TM</sup>. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred

embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of\_polypeptide that would\_be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4+ and/or CD8+ T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (e.g.,  $5 - 25 \mu g/ml$ ). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8+ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers

comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

#### **EXAMPLES**

#### **EXAMPLE 1**

## ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the Notl/Oligo-dT18 primer. Double-stranded cDNA was synthesized. ligated with EcoRI/BAX1 adaptors (Invitrogen, San Diego, CA) and digested with Notl. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64 x 10<sup>7</sup> independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 10<sup>6</sup> independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara et al. (Blood, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of

 $H_2O$ , heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl  $H_2O$  to form the driver DNA.

To form the tracer DNA, 10 μg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 μl H<sub>2</sub>O. Tracer DNA was mixed with 15 μl driver DNA and 20 μl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization {LH}). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μl H<sub>2</sub>O, mixed with 8 μl driver DNA and 20 μl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK\* (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ HD NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human

autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted

amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial oDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and

prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4283, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104; respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

# EXAMPLE 2 DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42  $^{\circ}$ C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that

F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression

in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### **EXAMPLE 3**

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' E. coli (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated

and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable.

Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold overexpression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.

Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

## EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water-{containing 0.1% TFA) may be used to elute the peptides. Following

lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

### **EXAMPLE 5**

## FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with Rsal according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat norvegicus cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to G. gallus dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

## EXAMPLE 6 PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100μg of P2S#12 and 120μg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 106 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10.5 M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of  $7\mu g/ml$  dextran sulfate and  $25\mu g/ml$  LPS for 3 days). Six days later, cells (5 x 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, Science 258:815-818, 1992) and 3 x 106/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were

restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, J. Immunol., 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5μg of P1S #10 and 120μg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2μ g/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7μg/ml dextran sulfate and 25μg/ml LPS for 3 days). Six days later cells (5 x 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Gells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly

basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

# EXAMPLE 7 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed in vitro to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (Critical Reviews in Immunology 18:65-75, 1998). The resulting CD8+ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon ELISPOT assay (see Lalvani et al., J. Exp. Med. 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 104 fibroblasts in the presence of 3  $\mu$ g/ml human  $\beta_2$ -microglobulin and 1  $\mu$ g/ml P2S-12 peptide or control E75 In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of y-interferon spots with increasing numbers of T

cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

### EXAMPLE 8

## PRIMING OF CTL IN VIVO USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

### **EXAMPLE 9**

## GENERATION OF HUMAN CTL IN VITRO USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using in vitro whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, The Journal of Immunology, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and

priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

# EXAMPLE 10 IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8+ T cells can be primed following repeated in vitro stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated in vitro with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary in vitro stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human in vitro priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis

with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

# EXAMPLE 11 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

# EXAMPLE 12 ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium-containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to

express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med. 186*:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

# EXAMPLE 13 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table 1 presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel Genes
r-cell gamma chain	P504S	23379 (SEQ
		ID NO:389)
		12 110.50)
Kallikrein	P1000C	
Vanikieni	PloodC	23399 (SEQ
		ID NO:392)
Vector	P501S	23320 (SEQ
		ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID	P503S	23381 (SEQ
NO:385)		ID NO:390)
PSA .	P510S	
Ald. 6 Dehyd.	P784P	
-iditol-2 dehydrogenase (23376; SEQ ID	P502S	
IO:388)		
Ets transcription factor PDEF (22672; SEQ	P706P	
D NO:398)	13.0	
TGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ	
	ID NO:396)	
	ID No.350)	
XIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID	
	NO:393)	4, 1
Prostatic Acid Phosphatase(22655; SEQ ID	P712P	
NO:397)		, i

transglutaminase (22611; SEQ ID NO:395)	P778P
HDLBP (23508; SEQ ID NO:394)	
CGI-69 Protein(23367; SEQ ID NO:387)	
KIAA0122(23383; SEQ ID NO:391)	
TEEG	*

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to-other-normal tissues-tested. It-was-over-expressed-in-67% of prostate-tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate

tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was overexpressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

## EXAMPLE 14 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA 95*:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Genter for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

<u>Table II</u>

<u>Prostate cDNA Libraries and ESTs</u>

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	- 11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

<u>Table III</u> Prostate Cluster Summary

Туре	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (i.e., the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

<u>Table IV</u> <u>Prostate-tumor Specific Clones</u>

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1-000C
402	22547	previously identified P704P

· · · · · · · · · · · · · · · · · · ·		
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

# EXAMPLE 15 FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel-genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

### EXAMPLE 16 FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

#### **CLAIMS**

- 1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;
- (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and
  - (c) complements of any of the sequence of (a) or (b).
- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.
- 3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.
- 4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

- 5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
- 9. An expression vector comprising a polynucleotide according to any one of claims 4-7.
- 10. A host cell transformed or transfected with an expression vector according to claim 9.
  - 11. An expression vector comprising a polynucleotide according claim 8.

- 12. A host cell transformed or transfected with an expression vector according to claim 11.
- 13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.
- 16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.
- 18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.
- 19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.
- 20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

- 22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.
- 23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.
- 24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.
- 27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.
- 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.
- 31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

- 32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.
- 34. A method according to any one of claims 29-32, wherein the caneer is prostate cancer.
- 35. A fusion protein comprising at least one polypeptide according to claim 1.
- 36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.
- 39. An isolated polynucleotide encoding a fusion protein according to claim 35.
- 40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.
- 41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.
- 42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

- 43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.
- 45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.
- 46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.
- 47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.
- 49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.
- 50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
  - (ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.

- 52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.
- 53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii); under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- An isolated T cell population, comprising T cells prepared according to the method of claim 53.
- 55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.
- 56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4<sup>+</sup> and/or CD8+ T cells isolated from a patient with at least one component selected from the group-consisting of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting-gell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T-cells, and thereby inhibiting the development of a cancer in the patient.

(ii);

- 57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4<sup>+</sup> and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
  - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
  - (iv) an antigen-presenting cell that expresses a polypeptide of (i) or

### such that T cells proliferate;

- (b) cloning at least one proliferated cell; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.
- 58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 59. A method according to claim 58, wherein the binding agent is an antibody.
- 60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

- 61. A method according to claim 58, wherein the cancer is prostate cancer.
- 62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 63. A method according to claim 62, wherein the binding agent is an antibody.
- 64. A method according to claim 63, wherein the antibody is a monoclonal antibody.
- 65. A method according to claim 62, wherein the cancer is a prostate cancer.
- 66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
  - 72. A diagnostic kit, comprising:
  - (a) one or more antibodies according to claim 21; and
  - (b) a detection reagent comprising a reporter group.

- 73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.
- 74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
- 77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.
- 78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
  - 79. A diagnostic kit, comprising:
  - (a) an oligonucleotide according to claim 77; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

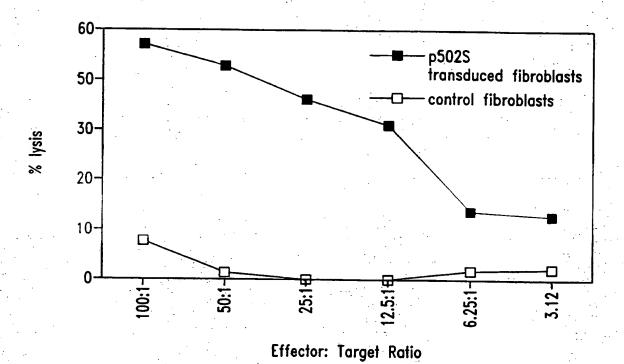


Fig. 1

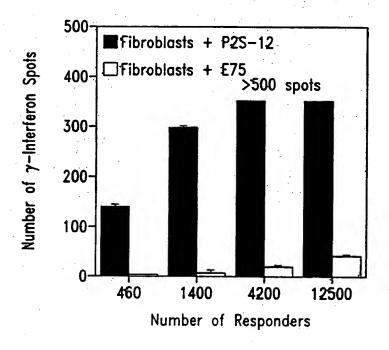


Fig. 2A

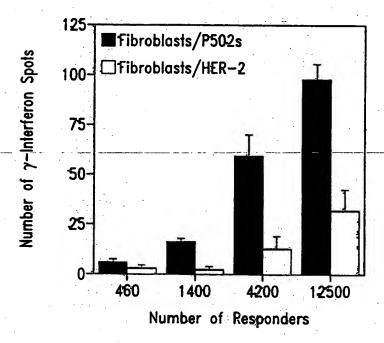
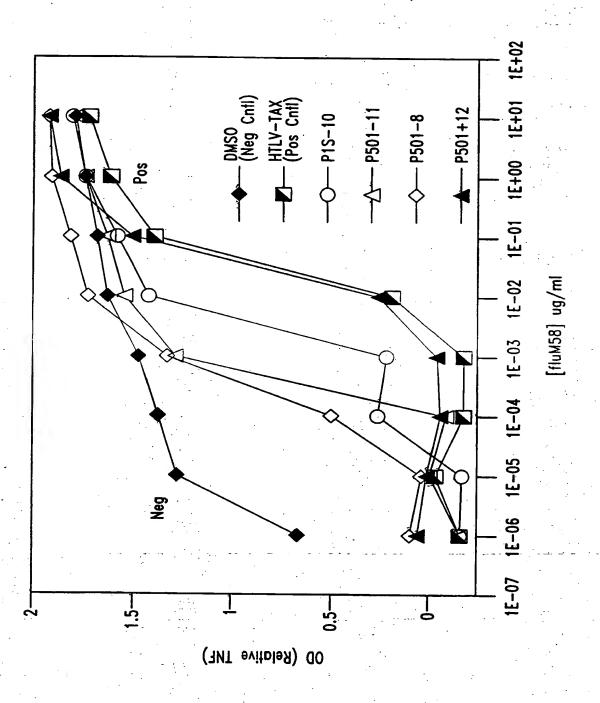


Fig. 2B

SUBSTITUTE SHEET (RULE 26)



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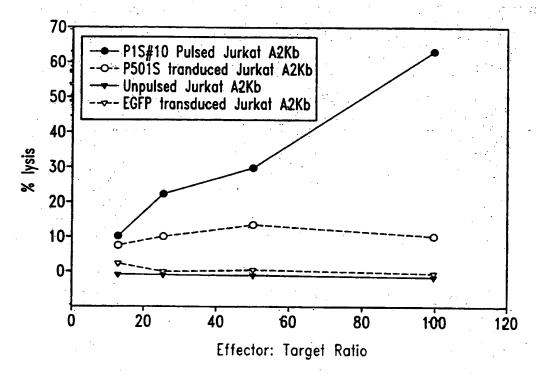
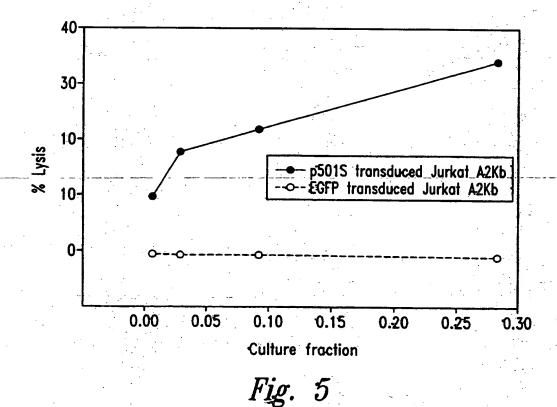
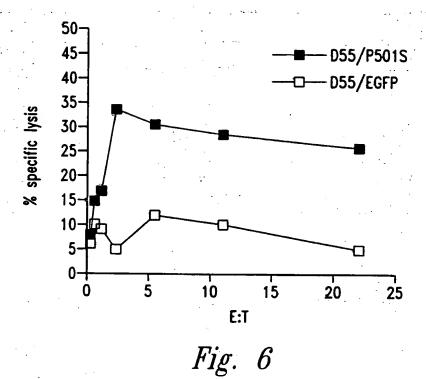
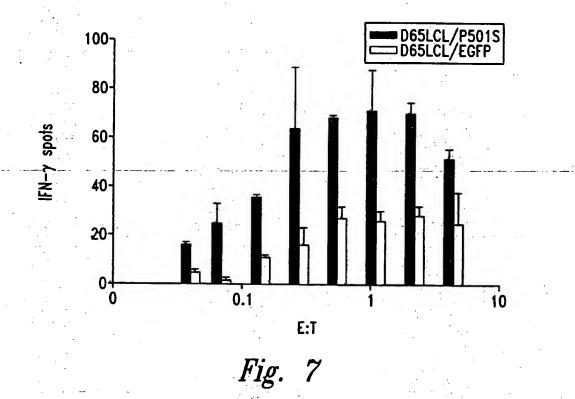


Fig. 4



SUBSTITUTE SHEET (RULE 26)





SUBSTITUTE SHEET (RULE 26)

#### SEQUENCE LISTING

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tegeteattg atcetngene eeggtetteg getgeggnga aeggtteact ceteaaagge
                                                                       780
ggtntnccgg ttatccccaa acnggggata cccnga
                                                                       816
      <210> 3
      <211> 773
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) . . . (773)
      <223> n = A,T,C or G
      <400> 3
cttttgaaag aagggatggc tgggggtgttt aacagcagag gtgcagggcg ggggctcacg
                                                                        60
tcctgctcct cactggtgat aaacgagccc cgttccttgt tgtgatcatg atgaacaacc
                                                                       120
tecteaaaag teagaacegg agteacacag geatetgtge egteaaagat ttgacaceae
                                                                       180
totgcottog tottotttgc aaatacatot gcaaacttot tottoattto tggccaatoa
                                                                       240
tccatgctca tctgattggg aagttcatca gactttagtc cannicctit gatcagcagc
                                                                       300
tcgtagaact ggggttctat tgctccaaca gccatgaatt ccccatctgc tgtcctgtaa
                                                                       360
gtcgtataga aaggtgctcc accatccaac atgttctgtc ctcgaggggg ggcccggtac
                                                                       420
ccaattcgcc ctatantgag tcgtattacg cgcgctcact ggccgtcgtt ttacaacgtc
                                                                       480
gtgactggga aaaccctggg cgttaccaac ttaatcgcct tgcagcacat ccccctttcg
                                                                       540
ccagctgggc gtaatancga aaaggcccgc accgatcgcc cttccaacag ttgcgcacct
                                                                       600
gaatgggnaa atgggacccc cctgttaccg cgcattnaac ccccgcnggg tttngttgtt
                                                                       660
acceccaent nnacegetta caettigeca gegeettane geoegeteee titeneetti
                                                                       720
cttecettee ttteneneen ettteeeeeg gggttteeee enteaaacee ena
                                                                       773
      <210> 4
      <211> 828
     _<212> DNA -------
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(828)
      <223> n = A,T,C or G
      <400> 4
cctcctgagt cctactgacc tgtgctttct ggtgtggagt ccagggctgc taggaaaagg
                                                                        60
aatgggcaga cacaggtgta tgccaatgtt tctgaaatgg gtataatttc gtcctctct
                                                                       120
teggaacact ggctgtetet gaagaettet egeteagttt eagtgaggae acacacaaag
                                                                       180
acgtgggtga ccatgttgtt tgtggggtgc agagatggga ggggtggggc ccaccctgga
                                                                       240
agagtggaca gtgacacaag gtggacactc tctacagatc actgaggata agctggagcc
                                                                       300
acaatgcatg aggcacacac acagcaagga tgacnctgta aacatagccc acgctgtcct
                                                                       360
```

540

```
gngggcactg ggaagcctan atnaggccgt gagcanaaag aaggggagga tccactagtt
ctanagegge egecacegeg gtgganetee anettttgtt ecetttagtg agggttaatt
gcgcgcttgg cntaatcatg gtcatanctn tttcctgtgt gaaattgtta tecgctcaca
                                                                       540
attccacaca acatacganc cggaaacata aantgtaaac ctggggtgcc taatgantga
                                                                       600
ctaactcaca ttaattgcgt tgcgctcact gcccgctttc caatcnggaa acctgtcttg
                                                                       660
concettgeat that gaaten gecaaceee ggggaaaage gettgegetet tgggegetet
                                                                       720
tecgetteet eneteantta ntecetnene teggteatte eggetgenge aaaceggtte
                                                                       780
accncctcca aagggggtat tccggtttcc ccnaatccgg gganancc
                                                                       828
      <210> 5
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 5
ttttttttt tttttactga tagatggaat ttattaagct tttcacatgt gatagcacat
                                                                        60
agttttaatt gcatccaaag tactaacaaa aactctagca atcaagaatg gcagcatgtt
                                                                       120
attttataac aatcaacacc tgtggctttt aaaatttggt tttcataaga taatttatac
                                                                       180
tgaagtaaat ctagccatgc ttttaaaaaaa tgctttaggt cactccaagc ttggcagtta
                                                                       240
acatttggca taaacaataa taaaacaatc acaatttaat aaataacaaa tacaacattg
                                                                       300
taggccataa tcatatacag tataaggaaa aggtggtagt gttgagtaag cagttattag
                                                                       360
aatagaatac cttggcctct atgcaaatat gtctagacac tttgattcac tcagcctga
                                                                       420
cattcagttt tcaaagtagg agacaggttc tacagtatca ttttacagtt tccaacacat
                                                                       480
tgaaaacaag tagaaaatga tgagttgatt tttattaatg cattacatcc tcaagagtta
                                                                       540
tcaccaaccc ctcagttata aaaaattttc aagttatatt agtcatataa cttggtgtgc
                                                                       600
ttattttaaa ttagtgctaa atggattaag tgaagacaac aatggtcccc taatgtgatt
                                                                       660
gatattggtc attittacca gcttctaaat ctnaactttc aggcttttga actggaacat
                                                                       720
tgnatnacag tgttocanag ttncaaccta ctggaacatt acagtgtgct tgattcaaaa
                                                                       780
tgttattttg ttaaaaatta aattttaacc tggtggaaaa ataatttgaa atna
                                                                       834
      <210> 6
      <211> 818
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (818)
      \langle 223 \rangle n = A,T,C or G
      <400> 6
ttttttttt tttttttt aagaceetca teaatagatg gagacataca gaaatagtea
                                                                        60
aaccacatct acaaaatgcc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga
                                                                       120
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagttg agccaataat
                                                                       180
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcgga
                                                                       240
aatggtgaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagacccag
                                                                       300
taaaattgta ataagcagtg citgaattat tiggitticgg tigtiticta tiagactatg
                                                                       360
gtgagctcag gtgattgata ctcctgatgc gagtaatacg gatgtgttta ggagtgggac
                                                                       420
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgccctccta gttgggggt
                                                                       480
aggggctagg ctggagtggt aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga
```

4

```
ggtaataaat aggattatcc cgtatcgaag gcctttttgg acaggtggtg tgtggtgcc
                                                                       600
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgttggg
                                                                       660
ttantanggo ctantatgaa gaacttttgg antggaatta aatcaatngo ttggooggaa
                                                                       720
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta cccnacccat
                                                                       780
ggaatnence ecceggaena ntgnatecet attettaa
                                                                       818
      <210> 7
      <211> 817
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(817)
      <223> n = A,T,C or G
      <400> 7
ttttttttt tttttttt tggctctaga gggggtagag ggggtgctat agggtaaata
                                                                        60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt
                                                                       120
ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcggtga
                                                                       180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaat gtggggacaq
                                                                       240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga
                                                                       300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg
                                                                       360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc
                                                                       420
attggtggcc aattgatttg atggtaaggg gagggatcgt tgaactcgtc tgttatqtaa
                                                                       480
aggatneett ngggatggga aggenatnaa ggaetangga thaatggegg geangatatt
                                                                       540
tcaaacngto totanttoot gaaacgtotg aaatgttaat aanaattaan tttngttätt
                                                                       600
gaatnttnng gaaaagggct tacaggacta gaaaccaaat angaaaanta atnntaangg
                                                                       660
cnttatentn aaaggtnata aceneteeta tnateeeace caatngnatt eeccaenenn
                                                                       720
acnattggat neceeantte canaaangge eneceeegg tgnanneene ettttgttee
                                                                       780
cttnantgan ggttattcnc ccctngcntt atcancc
                                                                       817
      <210> 8
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(799)
      <223> n = A, T, C or G
      <400> 8
catttccggg tttactttct aaggaaagcc gagcggaagc tgctaacgtg ggaatcggtg
                                                                        60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt
                                                                       120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag
                                                                       180
tacgaacage geetgaaagt getggagegg gaggteeage agtgtageeg egteetgggg
                                                                       240
tgggtggccg angectgane egetetgeet tgetgeeece angtgggeeg ceacecetg
                                                                       300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac ceccacangg
                                                                       360
ggattttgct cctanantaa ggctcatctg ggcctcggcc ccccacctg gttggccttg
                                                                       420
tetttgangt gagececatg tecatetggg ceaetgteng gaceaeettt ngggagtgtt
                                                                       480
ctccttacaa ccacannatg cccggctcct cccggaaacc anteccanec tgngaaggat
                                                                       540
caagneetgn atceactnnt netanaaceg geeneeneeg engtggaace encettntgt
                                                                       600
teettteent tnagggttaa tnnegeettg geettneean ngteetnene ntttteennt
                                                                       660
gttnaaattg ttangeneee neennteeen ennennenan eeegaeeenn annttnnann
                                                                       720
```

```
nectgggggt necnnengat tgaccennee necethtant tgenttnggg nnenntgece
                                                                        780
ctttccctct nggganncg
                                                                        799
      <210> 9
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A,T,C or G
      <400> 9
acgeettgat ceteceagge tgggaetggt tetgggagga geegggeatg etgtggtttg
                                                                        60
taangatgac actoccaaag gtggtootga cagtggcoca gatggacatg gggotoacot
                                                                       120
caaggacaag gccaccaggt gcgggggccg aagcccacat gatccttact ctatgagcaa
                                                                       180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang
                                                                       240
caggicatgg ggitgingne caactggggg ceneaaegea aaanggenea gggetengn
                                                                       300
cacccatece angaegegge tacactnetg gaecteeene tecaccaett teatgegetg
                                                                       360
ttentaceeg egnatnigie ecanetgitt engigeenae tecanettet nggaegigeg
                                                                       420
ctacatacgc ccggantene neteccgett tgteectate caegtneean caacaaattt
                                                                       480
encentanty cacenattee caenttine agnitteene nnegnette etintaaaaq
                                                                       540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn ccccctnata
                                                                       600
gctgaantcc ccatnaccnn gnctcnatgg ancentcent tttaannacn ttctnaactt
                                                                       660
gggaanance etegreenth ecceenttaa teceneettg enanghment ecceenntee
                                                                       720
nccommiting gentintiann chaaaaagge commancaa tetectinnen ceteantteq
                                                                       780
ccanccctcg aaatcggccn c
                                                                       801
     <210> 10
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
      <223> n = A,T,C or G
      <400> 10
cagtetaint ggccagigig geagettice eigiggeige eggigeeaca igecigteee
                                                                        6.0
acagtgtggc cgtggtgaca gcttcagocg coetcacegg gttcacette tcagocetqe
                                                                       120
agatectgee etacacactg geetecetet accaceggga gaageaggtg tteetgeeca
                                                                       180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc
                                                                       240
caggeectaa geetggaget ceetteecta atggacaegt gggtgetgga ggeagtggee
                                                                       300
tgctcccacc tecaccegeg etetgegggg cetetgeetg tgatgtetec gtacgtqtqq
                                                                       360
tggtgggtga geccaccgan gecagggtgg tteegggeeg gggcatetgc etggaceteg
                                                                       420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat
                                                                       480
tgtccagete agecagtetg teactgeeta tatggtgtet geegeaggee tgggtetggt
                                                                       540
eccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagog
                                                                       600
ttaaaaaatt ocagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc
                                                                       660
tectgttaac eccatgggge tgeeggettg geeggeaatt tetgttgetg ceaaantnat
                                                                       720
gtggctctct gctgccacct gttgctggct gaagtgcnta engeneanct nggggggtng
                                                                       780
ggngttecc
                                                                       789
```

```
<210> 11
      <211> 772
      <212> DNA
     <213> Homo sapien
     ·<220>
      <221> misc feature
      <222> (1)...(772)
      \langle 223 \rangle n = A,T,C or G
      <400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac
                                                                        60
tttgttaaat aaataagtta aatatttaaa tgcctgtgtc tctgtgatgg caacagaagg
                                                                        120
accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc
                                                                        180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata
                                                                        240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag
                                                                        300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt
                                                                        360
tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc
                                                                        420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc
                                                                        480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana
                                                                        540
aactggggaa aaaagaaaag gacgcccan cccccagctg tgcanctacg cacctcaaca
                                                                       600
gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca
                                                                       660
accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca
                                                                        720
ggcccnccac cccnaatntt gctgggaaat ttttcctccc ctaaattntt tc
                                                                       772
      <210> 12
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(751)
      <223> n = A.T.C or G
      <400> 12
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt_tccacacttg_agtgaagtct_tcctgggaac_cataatcttt_cttgatggca____
                                                                       300
ggcactacca gcaacgtcag ggaagtgctc agccattgtg gtgtacacca aggcgaccac
                                                                       360
agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc
                                                                       420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna
                                                                       480
enceggetge gatgaagaaa tnaceceneg ttgacaaact tgcatggcac tggganccac
                                                                       540
agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg
                                                                       600
ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct
                                                                       660
tnatnaacht gaaccetgen tngtggetee tgtteaggne ennggeetga ettetnaann
                                                                       720
aangaacten gaagneeeca enggananne g
                                                                       751
      <210> 13
      <211> 729
      <212> DNA
```

<213> Homo sapien

```
<220>
      <221> misc_feature
      <222> (1)...(729)
      <223> n = A,T,C or G
      <400> 13
gagecaggeg teectetgee tgeccaetea gtggcaacae cegggagetg ttttgteett
                                                                        60
tgtgganeet cagcagtnee etettteaga acteantgee aaganeeetg aacaggagee
                                                                       120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatctt
                                                                       180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt
                                                                       240
ctgaagatet tegggeeact gtegteeagt gecatgeagt ttgteaacgt gggetaette
                                                                       300
ctcatcgcag ccggcgttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag
                                                                       360
actgagagea agtgtgeeet egtgaegtte ttetteatee teeteeteat etteattget
                                                                       420
gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt
                                                                       480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt
                                                                       540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggattt
                                                                       600
gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa
                                                                       660
acgtocccaa cacagocaat tgaaaacctg cacccaaccc aaangggtoc ccaaccanaa
                                                                       720
attnaaggg
                                                                       729
      <210> 14
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220> ...
      <221> misc_feature
      <222> (1)...(816)
      <223> n = A,T,C or G
      <400> 14
tgctcttcct caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgcag
                                                                        60
tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct
                                                                       120
ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag
                                                                       180
ccactcgtgt attiticaca ggcagcctcg tecgacgcgt eggggcagtt gggggtgtet
                                                                       240
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga
                                                                       300
cangigecag ageacactgg atggegeett tecatgnnan gggeeetgng ggaaagteee
                                                                       360
tganccccan anctgcctct caaangcccc accttgcaca ccccgacagg ctagaatgga
                                                                       420
atcttettee egaaaggtag tinttettgt tgeecaance ancecentaa acaaactett
                                                                       480
gcanatctgc_tccgnggggg_tcntantacc_ancgtgggaa_aagaacccca_qqcnqcqaac_
                                                                       540-
caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna
                                                                       600
ctgtnnanct ttagncentg gtectentgg gttgnnettg aacetaaten cennteaact
                                                                       660
gggacaaggt aantngeent eetttnaatt eeenanentn eeeeetggtt tggggttttn
                                                                       720
cnenetecta ecceagaaan neegtgttee ecceeaacta ggggeenaaa cenntinte
                                                                       780
cacaaccetn ecceaccac gggttengnt ggttng
                                                                       816
      <210> 15
      <211> 783
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(783)
      <223> n = A,T,C or G
```

```
<400> 15
ccaaggeetg ggeaggeata nacttgaagg tacaaceeca ggaaceeetg gtgetgaagg
                                                                        60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga
                                                                        120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga
                                                                        180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca
                                                                        240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt
                                                                       300
teccaegetg gtactatgae eccaeggage agatetgeaa gagtttegtt tatggagget
                                                                       360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcngggtg
                                                                       420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct
                                                                       480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca
                                                                       540
ncaatggctg ctgcatcnac antitcctng aattgtgaca acacccccca ntgcccccaa
                                                                       600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccgg
                                                                       660
cncctccntt ttccccnntn aacaaagggc nctngcnttt gaactgcccn aacccnggaa
                                                                       720
tetneenngg aaaaantnee ecceetggtt eetnnaance ecteenenaa anetneecee
                                                                       780
                                                                       783
      <210> 16
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      \langle 223 \rangle n = A,T,C or G
      <400> 16
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtagggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca
                                                                       300
ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcgaccaca
                                                                       360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca
                                                                       420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg
                                                                       480
congotgoga atgaaagaaa ntacccacgt tgacaaactg catggccact ggacgacagt
                                                                       540
tggcccgaan atcttcagaa aagggatgcc ccatcgattg aacacccana tgcccactgc
                                                                       600
chacaggget geneenenen gaaagaatga gecattgaag aaggatente ntggtettaa
                                                                       660
tgaactgaaa centgeatgg tggeeeetgt teagggetet tggeagtgaa ttetganaaa
                                                                       720
aaggaacngc-ntnagccccc ccaaangana-aaacaccccc-gggtgttgcc ctgaattggc
                                                                       780
ggccaaggan ccctgccccn g
                                                                       801
      <210> 17
      <211> 740
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(740)
      <223> n = A,T,C or G
     <400> 17
gtgagagcca ggcgtccctc tgcctgccca ctcagtggca acacccggga gctgttttgt
                                                                        60
```

```
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg
                                                                        120
agecaccatg cagtgettea getteattaa gaccatgatg atcetettea atttgeteat
                                                                        180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc
                                                                        240
ctttctgaag atcttcgggc cactgtcgtc cagtgocatg cagtttgtca acgtgggcta
                                                                        300
cttcctcatc gcagocggcg ttgtggtctt tgctcttggt ttcctgggct gctatggtgc
                                                                        360
taagacggag agcaagtgtg coctcgtgac gttcttcttc atcctcctcc tcatcttcat
                                                                        420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattect
                                                                        480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc
                                                                        540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg
                                                                        600
gaattttgaa aganteneec tacttecaaa aaaaaanant tgeetttnee ecenttetgt
                                                                        660
tgcaatgaaa acntcocaan acngocaatn aaaacctgcc cnnncaaaaa ggntcncaaa
                                                                        720
caaaaaant nnaagggttn
                                                                        740
      <210> 18
      <211> 802
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(802)
      \langle 223 \rangle n = A,T,C or G
      <400> 18
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca
caaggictic cagcigoogo acattaogoa gggcaagago ciccagcaac acigcataig
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct
gageetetgt tagtggagga agatteeggg etteagetaa gtagteageg tatgteecat
                                                                       240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa
                                                                       300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat
                                                                       360
ggatgagtgt ggccagcgct gcccccttgg ocgacttggc taggagcaga aattgctcct
                                                                       420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg
                                                                       480
gctcaggatg tecagagacg tggttecgec cectenetta atgacacegn ccanneaace
                                                                       540
gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cnctacttgc
                                                                       600
aancttegte nggeeeatgg aatteacene aeeggaaetn gtangateea etnnttetat
                                                                       660
aaccggncgc caccgcnnnt ggaactccac tettnttncc tttacttgag ggttaaggte
                                                                       720
accettnineg tracettggt ccaaacentn centgrgteg anatngtnaa tenggnoena
                                                                       780
tnccancene atangaagee ng
                                                                       802
     <210> 19
      <211> 731
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(731)
      <223> n = A,T,C or G
      <400> 19
cnaagettee aggtnaeggg eegenaance tgaccenagg tancanaang eagnengegg
gageceaeeg teaegnggng gngtetttat nggagggge ggagecaeat enetggaent
                                                                       120
entgacecca actececnee nencantgea gtgatgagtg cagaactgaa ggtnacgtgg
                                                                       180
caggaaccaa gancaaanne tgeteennte caagteggen nagggggegg ggetggeeac
                                                                       240
geneateent enagtgetgn aaageeeenn cetgtetaet tgtttggaga aengennnga
```

```
catgeceagn gttanataac nggengagag tnantttgee tetecettee ggetgegean
                                                                       360
cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaatc tnccnccct
                                                                       420
ccactaaget cagaacaaaa aacttegaca ccacteantt gteacetgne tgeteaagta
                                                                       480
aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg
                                                                       540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc
                                                                       600
cnncnntcca aggggggnc ggccccaat cccccaacc ntnaattnan tttancccn
                                                                       660
ecceenggee eggeetttta enanentenn nnaengggna aaacennnge tttneceaae
                                                                       720
nnaatccncc t
                                                                       731
      <210> 20
      <211> 754
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(754)
      <223> n = A,T,C or G
      <400> 20
ttttttttt tttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc
                                                                        60
caaccccctc ntccaaatnn contttccgg gngggggttc caaacccaan ttanntttgg
                                                                       120
annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta
                                                                       180
tnancttnaa tncctggaaa congtngntt ccaaaaatnt ttaaccctta antocctccg
                                                                       240
aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc
                                                                       300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa
                                                                       360
ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg
                                                                       420
ganccenegg gaattaaegg ggnnnnteee thttgggggg enggnneece eccenteggg
                                                                       480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc
                                                                       540
ccaggntgag nntngggttt ncccccccc canggcccct ctcgnanagt tggggtttgg
                                                                       600
ggggcctggg atttintttc ccctnttncc tcccccccc ccnggganag aggttngngt
                                                                       660
tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga
                                                                       720
agtccnttgn agggntaaan ggccccctnn cggg
                                                                       754
      <210> 21
      <211> 755
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(755)
      <223> n = A,T,C or G
      <400> 21
atcaneccat gacccenaac nngggacene teaneeggne nnnenacene eggeenatea
                                                                       60
nngtnagnne actnennttn nateacneec encenactae gecenenane enaegeneta
                                                                      120
nncanatnee actganngeg egangtngan ngagaaanet nataccanag neaccanaen
                                                                      180
ecagetgtee nanaangeet nnnataengg nnnateeaat ntgnaneete enaagtattn
                                                                      240
nnenneanat gatttteetn anecgattae centnecece tanecectee cecceaacna
                                                                      300
egaaggenet ggneenaagg nngegnenee eegetagnte eeenneaagt eneneneeta
                                                                      360
aactcancen nattachege ttentgagta teactceecg aateteacee tactcaacte
                                                                      420
aaaaanaten gatacaaaat aatneaagee tgnttatnae aetntgaetg ggtetetatt
                                                                      480
ttagnggtcc ntnaanchtc ctaatacttc cagtctnect tenecaattt cenaangget
                                                                      540
ctttcngaca gcatnittig gitcccnnti gggitcitan ngaattgccc ticningaac
                                                                      600
```

```
gggctcntct tttccttcgg ttancctggn ttcnnccggc cagttattat ttcccntttt
                                                                        660
aaattentne entitantti tggenttena aacceegge ettgaaaaeg geeceetggt
                                                                        720
aaaaggttgt tttganaaaa tttttgtttt gttcc
                                                                        755
      <210> 22
     <211> 849
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(849)
      \langle 223 \rangle n = A,T,C or G
      <400> 22
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt
                                                                         60
acgcinggan taangcgacc cgantictag gannencect aaaatcanac tgigaagain
                                                                        120
atcctgnnna cggaanggtc accggnngat nntgctaggg tgnccnctcc cannnenttn
                                                                        180
cataacteng nggccctgcc caccacette ggcggcccng ngnccgggcc cgggtcattn
                                                                        240
gnnttaaccn cactnngcna neggttteen neceenneng accenggega teeggggtne
                                                                        300
tetgtettee cetgnagnen anaaantggg ceneggneee etttaceeet nnacaageea
                                                                        360
engeenteta neenengeee eccetecant nngggggaet geenannget eegttnetng
                                                                        420
nnacccennn gggtneeteg gttgtegant enacegnang ceanggatte enaaggaagg
                                                                        480
tgcgttnttg gcccctaccc ttcgctncgg nncacccttc ccgacnanga nccqctcccq
                                                                        540
enennegning cetenected caacaceege netentengt negginnege ecceaceege
                                                                        600
necetenane ngnegnanen eteeneenee gteteannea ecaeceegee ecqceaqqee
                                                                        660
ntcanceach ggnngaenng nagenennte geneegegen gegneneet egeenengaa
                                                                        720
ctnentengg ccantinege teaaneenna enaaaegeeg etgegeggee egnagegnee
                                                                        780
necteenega gteeteeegn etteenaeee angnntteen egaggacaen nnaeeeegee
                                                                        840
nncangcgg
                                                                        849
      <210> 23
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(872)
      \langle 223 \rangle n = A,T,C or G
      <400> 23
gegeaaacta tacttegete gnactegtge geetegetne tettteete egeaaceatg
                                                                        6.0
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca
                                                                       120
cacachenan aganaaatee netgeettee anagtanaen attgaaenng agaaceange
                                                                       180
nggcgaatcg taatnaggcg tgcgccgcca atntgtcncc gtttattntn ccagcntonc
                                                                       240
ctnccnaccc tacntetten nagetgtenn acceetngtn egnaceeece naggteggga
                                                                       300
tegggttinn nntgacegng ennecette eccentecat nacganeene ecgcaceace
                                                                       360
nanngenege neecegnnet ettegeenee etgteetnin eccetginge etggenengn
                                                                       420
accgcattga cectegeenn ctnenngaaa negnanaegt cegggttgnn annanegetg
                                                                       480
tgggnnngcg tetgeneege gtteetteen nennetteea ecatettent taengggtet
                                                                       540
conceents tennicaens cetaggacge intectning ecceptinas tecceents
                                                                       600
egnegtgnee egneeceace nteatttnea naegntette acaannneet ggntnnetee
                                                                       660
chancing gtcancenag ggaagggngg ggnneenntg nttgacgttg nggngangte
                                                                       720
cgaanantee tencentean enctaceeet egggegnnet etengttnee aacttaneaa
                                                                       780
```

```
ntetecceeg ngngemente teageetene ceneceenet etetgeantg thetetgete
                                                                        840
tnaccnntac gantnttcgn cnccctcttt cc
                                                                       872
      <210> 24
      <211> 815
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(815)
      <223> n = A,T,C or G
      <400> 24
gcatgcaage ttgagtatte tatagngtea ectaaatane ttggentaat catggtenta
                                                                        60
nctgncttcc tgtgtcaaat gtatacnaan tanatatgaa tctnatntga caaganngta
                                                                       120
tentneatta gtaacaantg tnntgteeat eetgtengan canatteeca tnnattnegn
                                                                       180
cgcattenen geneantatn taatngggaa ntennntnnn neacenneat etatentnee
                                                                       240
genecetgae tggnagagat ggatnantte tnntntgace nacatgttea tettggattn
                                                                       300
aananecece egengneeae eggttngnng enageennte ecaagacete etgtggaggt
                                                                       360
aacctgcgtc aganncatca aacntgggaa acccgcnncc angtnnaagt ngnnncanan
                                                                       420
gatecegtee aggnttnace atceettene agegeeecet tingtgeett anagngnage
                                                                       480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc
                                                                       540
gaacccccta gggggantna thcaaanccc caggattgtc chchcangaa atccchcanc
                                                                       600
cccnccctac connettigg gacngtgacc aantecegga ginecagied ggeengnete
                                                                       660
ccccaccggt nnccntgggg gggtgaanct cngnntcanc cngncgaggn ntcgnaagga
                                                                       720
accggneeth ggnegaanng anenntenga agngeenent egtataacce eccetencea
                                                                       780
nccnacngnt agntccccc cngggtncgg aangg
                                                                       815
      <210> 25
      <211> 775
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(775)
      <223> n = A,T,C or G
      <400> 25
ecgagatgte tegeteegtg geettagetg tgetegeget actetetet tetggeetgg
                                                                        60
aggetateca gegtaeteca aagatteagg tttaeteacg teatecagea gagaatggaa
                                                                       120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact
                                                                       180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg
                                                                       240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg
                                                                       300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca
                                                                       360
tgtaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt
                                                                       420
ctgcttgctt gcnttttaat antgatatgc ntatacaccc taccctttat gnccccaaat
                                                                       480
tgtaggggtt acatnantgt tenentngga catgatette etttataant cencentteg
                                                                       540
aattgeeegt enceengttn ngaatgttte ennaaceaeg gttggeteee eeaggtenee
                                                                       600
tettaeggaa gggeetggge enetttneaa ggttggggga acenaaaatt tenettntge
                                                                       660
conceencea ennicitigng nnencantit ggaaccette enatteceet tggeetenna
                                                                       720
nccttnncta anaaaacttn aaancgtngc naaanntttn acttcccccc ttacc
                                                                       775
```

```
<211> 820
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(820)
       <223> n = A,T,C or G
       <400> 26
 anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat
                                                                         60
 cccanagata nettatanea acagtgettt gaccaagage tgetgggeac atttectgea
                                                                        120
 gaaaaggtgg cggtccccat cactcctcct ctcccatagc catcccagag gggtgagtag
                                                                        180
 ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca
                                                                        240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg gggtggcana nganagccta
                                                                        300
nctgagggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc
                                                                        360
ttectaeetg acnaecagng acennnaact gengeetggg gacagenetg ggancageta
                                                                        420
acnnageact cacctgcccc cccatggccg tncgcntccc tggtcctgnc aagggaagct
                                                                        480
ccctgttgga attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann
                                                                        540
gatggaattt thecetteeg geennteece tetteettta caegeeecet nntactente
                                                                        600
teeetetntt nteetgnene aettttnaee cennnattte eettnattga teggannetn
                                                                        660
ganattecac thncgcctnc chtchatchg naanachaaa nacthtctna cccnggggat
                                                                        720
gggnncctcg ntcatcctct ctttttcnct accnccnntt ctttgcctct ccttngatca
780tccaacente gntggeentn ecceccennn teetttneee
820
       <210> 2.7
       <211> 818
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(818)
       <223> n = A,T,C or G
       <400> 27
tetgggtgat ggeetettee teeteaggga eetetgactg etetgggeea aagaatetet
                                                                        60
tgtttcttct ccgagcccca ggcagcggtg attcagccct gcccaacctg attctgatga
                                                                        120
ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc.
                                                                        180
ctgctgagca cttccgcccc tcaccctgcc cagcccctgc catgagctct gggctgggtc
                                                                        240
tecgeeteca gggttetget ettecangea ngecaneaag tggegetggg ceacactgge
                                                                        300
ttcttcctgc ccentccctg gctctgantc tctgtcttcc tgtcctgtgc angenecttg
                                                                        360
gateteagtt teectenete anngaactet gtttetgann tetteantta aetntgantt
                                                                        420
tatnacenan tggnetgtne tgtennactt taatgggeen gaeeggetaa teeeteete
                                                                        480
netecettee antiennnna accngettne ententetee centaneceg cengggaane
                                                                        540
ctcctttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc
                                                                        600
etgntnnece enetenennt theetegtee ennennegen nngeanntte nengteeenn
                                                                        660
tnnctctten ngtntegnaa ngntenentn tnnnnngnen ngntnntnen teettetene
                                                                        720
connitgiang thattannac acaganeece annacianna aggainstina tetreneage
                                                                        780
cccnnccccc ngnattaagg cctccnntct ccggccnc
                                                                        818
       <210> 28
      <211> 731
      <212> DNA
```

<213> Homo sapien

```
<220>
      <221> misc_feature
      <222> (1)...(731)
      <223> n = A,T,C or G
      <400> 28
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg
                                                                        60
teceaacatg anggtgnngt tetettttga angagggttg ngtttttann eenggtgggt
                                                                       120
gattnaaccc cattgtatgg agnnaaaggn tttnagggat ttttcggctc ttatcagtat
                                                                       180
ntanattcct gtnaatcgga aaatnatntt tcnncnggaa aatnttgctc ccatccgnaa
                                                                       240
attrictcccg ggtagtgcat nttngggggn engecangtt teccaggetg ctanaategt
                                                                       300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn tacccgactg
                                                                       360
tnnnttncct tcgccctntg actctgcnng agcccaatac ccnngngnat gtcncccngn
                                                                       420
nnngcgncnc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn
                                                                       480
cgtttcncat naaggcactt tngcctcatc caaccnctng ccctcnncca tttngccgtc
                                                                       540
nggttenect aegetnntng encetnnntn ganattttne eegeetnggg naanceteet
                                                                       600
gnaatgggta gggnettnic tittnacenn gnggintact aatenneine acgeninett
                                                                       660
tctcnacccc ccccttttt caatcccanc ggcnaatggg gtctccccnn cgangggggg
                                                                       720
nnncccannc c
                                                                       731
      <210> 29
      <211> 822
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc_feature
      <222> (1) ... (822)
      <223> n = A,T,C or G
      <400> 29
actagtecag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat
                                                                        60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt
                                                                       120
aththtache teatanneet ennnaceeae teeetettaa ecentaetgt geetatngen
                                                                       180
thnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc
                                                                       240
tenecatnin geetananta ngineatace etatacetae necaatgeta nnnetaanen
                                                                       300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc
                                                                       360
tactctgact cccacngcct annnattagc anchtccccc nacnathtct caaccaaatc
                                                                       420
ntcaacaacc tatctanctg ttcnccaacc nttncctccg atccccnnac aaccccctc
                                                                       480
ccaaataccc nccacctgac ncctaacccn caccatcccg gcaagccnan ggncatttan
                                                                       540
ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccctaana
                                                                       600-
aatneteetn naatttaetn neantneeat caaneeeaen tgaaaennaa eeeetgtttt
                                                                       660
tanatecett etttegaaaa eenaceettt annneeeaac etttngggee eeceenetne
                                                                       720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg
                                                                       780 -
canatectat ceettanttn ggggneeett neeengggee ee
                                                                       822
      <210> 30
      <211> 787
```

<212> DNA

<220>

<213> Homo sapien

<221> misc\_feature

```
<222> (1)...(787)
     <223> n = A,T,C or G
      <400> 30
eggeegeetg etetggeaca tgeeteetga atggeateaa aagtgatgga etgeecattq
                                                                         60
ctagagaaga cettetete tactgteatt atggageect geagactgag ggeteecett
                                                                        120
gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna
                                                                       180
getggaagee etggagggee tetetegeea geeteeeet teteteeaeg etetecangg
                                                                       240
acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga
                                                                       300
cccatggggc ctgnaaggcc agggtetect ttgacaccat ctctcccgtc ctgcctggca
                                                                       360
ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt
                                                                       420
tecenttaat gaaggttaat tgenegettg gegtaateat nggteanaac tnttteetgt
                                                                       480
gtgaaattgt ttntcccctc ncnattccnc ncnacatacn aacccggaan cataaagtgt
                                                                       540
taaageetgg gggtngeetn nngaatnaac tnaactcaat taattgegtt ggeteatgge
                                                                       600
ecgettteen ttenggaaaa etgtenteee etgenttnnt gaateggeea eeceeenggg
                                                                       660
aaaageggtt tgenttttng ggggnteett cenetteece eetenetaan ceetnegeet
                                                                       720
eggtegttne nggtngeggg gaangggnat nnneteeene naagggggng agnnngntat
                                                                       780
ccccaaa
                                                                       787
      <210> 31
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>.
      <221> misc feature
      <222> (1)...(799)
      \langle 223 \rangle n = A,T,C or G
      <400> 31
ttttttttt ttttttggc gatgctactg tttaattgca ggaggtgggg gtgtgtgtac
                                                                        60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc
                                                                       120
aacaaaggac teetgeagee ttetetgtet gtetettgge geaggeacat ggggaggeet
                                                                       180
cccgcagggt gggggccacc agtocagggg tgggagcact acanggggtg ggagtgggtg
                                                                       240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca
                                                                       300
ggggaccttc tgttctccca nggnaacttc ntnnatctcn aaagaacaca actgttctt
                                                                       360
engeanttet ggetgtteat ggaaageaca ggtgteenat tinggetggg acttggtaca
                                                                       420
tatggttccg gcccacctct cocntcnaan aagtaattca ccccccccn centetnttg
                                                                       480
cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg
                                                                       540
ntnateneen eetgaangeg eeaagttgaa aggeeaegee gtneeenete eecatagnan
                                                                       600
nttttnnent canctaatge ecceeengge aacnatecaa teeceeecen tgggggeece
                                                                       660
ageccangge eccegneteg ggnnneengn enegnantee ecaggntete ecantengne
                                                                       720
conningence eeegeacgea gaacanaagg ningageene egeanninnin negtinenae
                                                                       780
ctcgccccc ccnncgnng
                                                                       799
      <210> 32
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
```

<223> n = A,T,C or G

```
<400> 32-
60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac
                                                                     120
ggcaacaggc teeggeggeg geggeggegg ceetacetge ggtaccaaat ntgcageete
                                                                     180
cgctcccgct tgatnttcct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn
                                                                     240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc
                                                                     300
nattaggaat agtggtntta cocnconceg ttggcncact cocontggaa accacttnto
                                                                     360
geggeteegg catetggtet taaacettge aaacnetggg gecetettt tggttantnt
                                                                     420
ncengecaca atcatnacte agaetggene gggetggece caaaaaanen ecceaaaace
                                                                     480
ggnccatgtc ttnncggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac
                                                                     540
ccaaaagttc ttgnggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcatc
                                                                     600
ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt
                                                                     660
tggnnggcaa gntggnteec cettegggee eeeggtggge cennetetaa ngaaaacnee
                                                                     720
ntcctnnnca ccatccccc nngnnacgnc tancaangna tcccttttt tanaaacggg
                                                                     780
cccccncg
                                                                     789
      <210> 33
      <211> 793
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(793)
      <223> n = A,T,C or G
      <400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg
                                                                      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg
                                                                     120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana
                                                                     180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg
                                                                    240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca
                                                                     300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac
                                                                     360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc
                                                                    420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct
                                                                    480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac
                                                                    540
acaacatacg anceggaage atnaaatttt aaageetggn ggtngeetaa tgantgaact
                                                                    600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt
                                                                    660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg
                                                                    720
cgcncttccc gctttctcgc ttcctgaant ccttccccc ggtctttcgg cttgcggcna
                                                                    780
acggtatcna cct
                                                                     793
      <210> 34
      <211> 756
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(756)
      <223> n = A,T,C or G
      <400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg
```

```
ccaaccacag ggaccaaget gaccaaacag cagetaatte tggcccgtga catactggag
                                                                       180
atoggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatqqcc
                                                                       240
cageteaaat getaetaett tgattacaan gageagetee eegagteage etatatgeae
                                                                       300
cagetettgg geeteaacet eetetteetg etgteecaga acegggtgge tgantnecae
                                                                       36Ò
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca
                                                                       420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcctgg ccnagggtaa
                                                                       480
catcccccgc cgagagetac accttettea ttgacateet getegacaet atcagggatg
                                                                       540
aaaatcgcng ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg
                                                                       600
athenetagt netagaateg geoegecate geggtggane etecaacett tegttheeet
                                                                       660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acncengttn cctgtgttga
                                                                       720
aattnttaac ccccacaat tccacgccna cattng
                                                                       756
      <210> 35
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 35
ggggatetet anatenacet gnatgeatgg ttgteggtgt ggtegetgte gatgaanatg
                                                                        60
aacaggatet tgecettgaa getetegget getgtnttta agttgeteag tetgeegtea
                                                                       120
tagicagaca enetetiggg caaaaaacan daggaintga gietigatti cacetecaat
                                                                       180
aatcttengg getgtetget eggtgaacte gatgaenang ggeagetggt tgtgtntgat
                                                                       240
aaantccanc angtteteet tggtgacete eeetteaaag ttgtteegge etteateaaa
                                                                       300
ettetnnaan angannance cancettegte gagetggnat tegganaaca egteaceget
                                                                       360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt
                                                                       420
ggeneaaate egacteeen teettgaaag aageenatea caceeecte eetggactee
                                                                       480
nncaangact ctnccgctnc cccntccnng cagggttggt ggcannccgg gcccntgcgc
                                                                       540
ttetteagee agtteaenat ntteateage ecetetgeea getgttntat teettggggg
                                                                       600
ggaancegte tetecettee tgaannaact ttgaccgtng gaatageege gentencent
                                                                       660
achtnetggg eegggtteaa anteetteen ttgmennten eetegggeea ttetggattt
                                                                       720
nccnaacttt tteetteece enceeenegg ngtttggntt ttteatnggg ceeeaactet
                                                                       780
getnttggee anteceetgg gggentntan eneceeetnt ggteeentng ggee
                                                                       834
      <210> 36
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(814)
      <223> n = A,T,C or G
      <400> 36
cggncgcttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn
                                                                       €0
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca
                                                                       120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggtctctcc acccctgta
                                                                       180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact
                                                                       240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca
                                                                       300
ctaaaacanc ccagegetca ettetgettg ganaaatatt etttgetett ttggacatca
                                                                       360
```

```
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc
                                                                       420
antganetgg aaggeetgaa nettagtete caaaagtete ngeecacaag accqccace
                                                                       480
aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag
                                                                       540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc
                                                                       600
cttccggtct gatccnaaag gaatgttcct gggtcccant ccctcctttg ttncttacgt
                                                                       660
tgtnttggac contgetngn atnacecaan tganatecec ngaageacec tneeetgge
                                                                       720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcnccnaan
                                                                       780
ggngaactca agaaggtctn ngaaaaacca cncn
                                                                       814
      <210> 37
      <211> 760
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(760)
      \langle 223 \rangle n = A,T,C or G
      <400> 37
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg
                                                                        60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt gcagagtcct
                                                                       120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg
                                                                       180
tenaanceae tegtgtattt tteacangea geeteeteeg aagenteegg geagttgggg
                                                                       240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt
                                                                       300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat
                                                                       360
encethance caaactgeet etcaaaggee acettgeaca eccegacagg etagaaatge
                                                                       420
actitititic ccaaaggtag tigititigi igcccaagca nectecanea aaccaaaane
                                                                       480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccggcngn
                                                                       540
ganceneett gtttgaatge naaggnaata ateeteetgt ettgettggg tggaanagea
                                                                       600
caattgaact gttaacnttg ggccgngttc cnctngggtg gtctgaaact aatcaccgtc
                                                                       660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtnnttt
                                                                       720
ctcctctncc ctaaaaatcg tnttcccccc ccntanggcg
                                                                       760
      <210> 38
      <211> 724
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(724)
      <223> n = A,T,C or G
      <400> 38
ttttttttt tttttttt tttttttt tttttaaaaa ccccctccat tgaatgaaaa
                                                                        60
cttccnaaat tgtccaaccc cctcnnccaa atnnccattt ccgggggggg gttccaaacc
                                                                       120
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa
                                                                       180
aatttaaccc attatnaact taaatneetn gaaaccentg gnttecaaaa atttttaace
                                                                       240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaaggtt
                                                                       300
ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt
                                                                       360
tectnttaan entnggtaac teeegntaat gaannneeet aanceaatta aacegaattt
                                                                       420
tttttgaatt ggaaatteen ngggaattna ceggggtttt tecentttgg gggeeatnee
                                                                       480
cccnctttcg gggtttgggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana
                                                                       540
aaaaaactcc caagnnttaa ttngaatntc ccccttccca ggccttttgg gaaaggnggg
                                                                       600
```

```
tttntggggg cengggantt entteeceen ttneeneece coccoenggt aaanggttat
                                                                       660
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccgggncg
                                                                       720
gccg
                                                                       724
      <210> 39
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(751)
      <223> n = A,T,C or G
      <400> 39
ttttttttt tttttttt ctcacattta atttttattt tgatttttt taatgctgca
                                                                        6.0
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt
                                                                       120
tttatttatt tttactgaaa gtgagaggga acttttgtgg cctttttcc ttttctgta
                                                                       180
ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aaggqqqttt
                                                                       240
cgcaaaatca ctcgggggaa nggaaaggtt gctttgttaa tcatgcccta tggtgggtga
                                                                       3:00
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc tttaattana
                                                                       360
cttgggggtt ccctccccan accaaccccn ctgacaaaaa gtgccngccc tcaaatnatg
                                                                       420
tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa
                                                                       480
tgaagggtta ccatntttaa enceacetee aentggennn geetgaatee tenaaaanen
                                                                       540
coctdaanon aattnotning cocoggione gentinigtor enecoggget coggaanin
                                                                       600
caccccnga annonninc naacnaaatt cogaaaatat toconniono toaattooco
                                                                       660
cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgnnc cnnaaaatgn
                                                                       720
nnnnencete enetngteen naateneean e
                                                                       751
      <210> 40
      <211> 753
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(753)
      <223> n = A,T,C or G
      <400> 40
gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat
                                                                        60
agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg
                                                                       120
cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa
                                                                       180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact
                                                                       240
tetcaaagtt eeaggeaacn tegttgegac acaeeggaga eeaggtgatn agettggggt
                                                                       3.00
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna
                                                                       360
ataaaaggtg cgccccgca ccgttcanct cgcacttctc naanaocatg angttgggct
                                                                       420
chaacceace accanneegg actteettga nggaatteec aaatetette gntettegge
                                                                       480
ttetnetgat geectanetg gttgeoengn atgecaanea neeceaanee eeggggteet
                                                                       540
asancaccon cotoctentt teatotgggt thtthteeoc ggacentggt tectoteaaq
                                                                       600
ggancccata tetenacean tacteacent neceeceent gnnacecane ettetanngn
                                                                       660
tteecneecg nectetggee enteaaanan gettneacna eetgggtetg eetteecee
                                                                       720
tnecetatet gnacecenen tttgtetean tnt
                                                                       753
```

```
<211> 341
      <212> DNA
      <213> Homo sapien
      <400> 41
actatateca teacaacaga catgetteat eccatagaet tettgacata getteaaatg
agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac
                                                                        120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt
                                                                        180
tatagettgt ttaegtagta agtttttgaa gtetacatte aateeagaea ettagttgag
                                                                        240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat
                                                                        300
ttttactttt tgattaattg tgttttatat attagggtag t
                                                                        341
      <210> 42
      <211> 101
      <212> DNA
      <213> Homo sapien
      <400> 42
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat
                                                                         60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a
                                                                        101
      <210> 43
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 43
acatettigt tacagictaa gaigigitet taaateacea ticetteeig gieeteacee
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat
                                                                        120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca
                                                                        180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat
                                                                        240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cgggggccgc
                                                                        300
tcgaa
                                                                        305
      <210> 44
      <211> 852
      <212> DNA
      <213> Homo sapien
     ~<220>
      <221> misc_feature
      <222> (1)...(852)
      \langle 223 \rangle n = A,T,C or G
      <400> 44
acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt
                                                                       120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct
                                                                        180
ccagaatttc tcttttgtag taatatctca tagctcggct gagcttttca taggtcatgc
                                                                       240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga
                                                                       300
agacgccctc agatcggtct tcccatttta ttaatcctgg gttcttgtct gggttcaaga
                                                                       360
ggatgtcgcg gatgaattcc cataagtgag tccctctcgg gttgtgcttt ttggtgtggc
                                                                       420
acttggcagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca ggaaggtgac
                                                                       480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg
                                                                       540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatggaag
```

```
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc
                                                                        660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg
                                                                        720
ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact
                                                                        780
cntggaaagg gatacaattg gcatocagct ggttggtgtc caggaggtga tggagccact
                                                                        840
cccacacctg gt
                                                                        852
      <210> 45
      <211> 234
      <212> DNA
      <213> Homo sapien
      <400> 45
acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg
                                                                         60
agtetgacae cateeggage atcageattg ettegeagtg ecetacegeg gggaactett
                                                                        120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg
                                                                        180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacccg ctgt
                                                                        234
      <210> 46
      <211> 590
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature.
      <222> (1)...(590)
      <223> n = A,T,C or G
      <400> 46
actitttatt taaatgitta taaggcagat ctatgagaat gatagaaaac atggtgta
                                                                        60
atttgatage aatattttgg agattacaga gttttagtaa ttaccaatta cacagttaaa
                                                                        120
aagaagataa tatattocaa goanatacaa aatatotaat gaaagatoaa ggoaggaaaa
                                                                        180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta
                                                                        24.0-
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat
                                                                        300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat
                                                                       360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc
                                                                       420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag
                                                                        480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct
                                                                       540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt
                                                                       590
      <210> 47
      <211> 774
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (774)
      \langle 223 \rangle n = A,T,C or G
      <400> 47
acaagggggc ataatgaagg agtggggana gattttaaag aaggaaaaaa aacgaggccc
                                                                       60
tgaacagaat tttcctgnac aaeggggctt caaaataatt ttcttgggga ggttcaagac
                                                                       120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg
                                                                       180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa
                                                                       240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct
                                                                       300
```

```
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctcctgtgtg
                                                                        360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc
                                                                        420
ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt
                                                                        480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc
                                                                        540
acggcatggg aagcetttet gacttgeetg attacteeag catettggaa caateettga
                                                                        600
ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttggagcc
                                                                        660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct
                                                                        720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt
                                                                        774
       <210> 48
      <211> 124
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(124)
      <223> n = A,T,C or G
      <400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt
                                                                        60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact
                                                                       120
tggt
                                                                       124
      <210> 49
      <211> 147
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(147)
      <223> n = A,T,C or G
      <400> 49
gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt
                                                                        60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt
                                                                       120
ttagggcacc catatcccaa gcantgt
      <210>.50
      <211>...107
      <212> DNA
      <213> Homo sapien
      <400> 50
acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatattgc
                                                                        60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt
                                                                       107
      <210> 51
      <211> 204
      <212> DNA
      <213> Homo sapien
      <400> 51
gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg
```

```
cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag
                                                                       120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttggcca
                                                                       180
cctccctttt gggaccagca atgt
                                                                       204
      <210> 52
      <211> 491
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(491)
      <223> n = A,T,C or G
      <400> 52
acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta
                                                                        60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca
                                                                       120
ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa
                                                                       180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt
                                                                       240
tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtncc ctcagtccca
                                                                       3.00
atgitgcica gataaataaa tcicgigaga acttaccacc caccacaagc tticiggggc
                                                                       360
atgeaacagt gtetttett thettttet ttttttttt ttacaggeac agaaacteat
                                                                       420
caattttatt tggataacaa agggtctcca aattatattg aaaaataaat ccaagttaat
                                                                       480
atcactcttg t
                                                                       491
      <210> 53
      <211> 484
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc feature
      <222> (1)...(484)
      <223> n = A.T.C or G
      <400> 53
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga
                                                                       60
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac
                                                                       120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct
                                                                       180
caatcaaatc totacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct
                                                                       240
gcactagtat anacegetee tgteaggata anactgettt ggaacagaaa gggaaaaane
                                                                       300
agetttgant ttetttgtge tgatangagg aaaggetgaa ttacettgtt geeteteet
                                                                       360
aatgattggc aggtenggta aatnecaaaa catattecaa etcaacaett etttteeneg
                                                                       420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc
                                                                       480
                                                                       484
      <210> 54
      <211> 151
      <212> DNA
      <213> Homo sapien
     <400> 54
actaaacctc gtgcttgtga actccataca gaaaacggtg ccatccctga acacggctgg
                                                                      60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag
                                                                       120
tctatgtcct ctcaagtgcc tttttgtttg t
                                                                       151
```

```
<210>.55
       <211> 91
       <212> DNA
       <213> Homo sapien
       <400> 55
acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc
                                                                        60
gccctccagt ggatactcga gccaaagtgg t
                                                                        91
      <210> 56
      <211> 133
      <212> DNA
      <213> Homo sapien
      <400> 56
ggcggatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact
                                                                        60
tggatttttg gtatctgtgg gttgggggga cggtccagga accaataccc catggatacc
                                                                       120
aagggacaac tgt
                                                                       133
      <210> 57
      <211> 147
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(147)
      <223> n = A,T,C or G
      <400> 57
actctggaga acctgageeg etgeteegee tetgggatga ggtgatgean gengtggege
                                                                        60
gactgggage tgagecette cetttgegee tgeetcagag gattgttgee gacntgcana
                                                                       120
tctcantggg ctggatncat gcagggt
                                                                       147
      <210> 58
      <211> 198
      <212> DNA
      <213> Homo sapien
_ : . . . <220>
     <221> misc feature
      <222> (1)...(198)
      <223> n = A,T,C or G
      <400> 58
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc
                                                                       60
tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta
                                                                       120
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt
                                                                       180
ttgacttcta agtttggt
                                                                       198
      <210> 59
      <211> 330
      <212> DNA
      <213> Homo sapien
```

<400> 59		
acaacaaatg ggttgtgagg aagtcttatc ccattgaaaa ttatcattaa tgattttaaa cacctgtgct agcttgctaa aatgggagtt tacagtcaat aaatgacaaa gccagggcct cagaaggaat ctatttatc acatggatct tttcgtctt attggacttc tttgaagagt	tgacaagtta tcaaaaact aactctagag caaatatag acaggtggtt tccagactt	c actcaattt 12 t atcttctgaa 18 t ccagacccag 24
<210> 60	••	
<211> 175		
<212> DNA		
<213> Homo sapien		
400 60		
<400> 60		
accgtgggtg ccttctacat tcctgacggc gtcgtgggct ccttcctctt catcctcatc tcctggaacc agcggtggct gggcaaggcc	cagctggtgc tgctcatcg	a ctttgcgcac 120
•		
<210> 61	·	
<211> 154	·	
<212> DNA		
<213> Homo sapien		
<400> 61		
accccacttt tcctcctgtg agcagtctgg	acticicact octacatos	t
ggttgttgct cttcaacagt atcctccct	ttccagatet actasacea	t gagggtgagt 6(
tggactgcac agccccgggg ctccacattg	c <b>tg</b> t	g acagcagtgc 120 <b>154</b>
<210> 62		
<211> 30		
<212> DNA		
<213> Homo sapien		
	- 35	
<400> 62	*	
cgctcgagcc ctatagtgag tcgtattaga		3.0
<210> 63		
<211> 89		•
<212> DNA	<u> </u>	
<213> Homo sapien		
<400> 63	•	
acaagtcatt tcagcaccct ttgctcttca a	aaactgaoca tetttata	t ttaatgette 60
ctgtatgaat aaaaatggtt atgtcaagt		89
<210> 64	-90-	•
<211> 97		
<212> DNA	•	
<213> Homo sapien		· .
<400> 64		
accggagtaa ctgagtcggg acgctgaatc t aatcagtgca tccaggattg gtccttggat (	gaateeace aataaataaa tggggt	a ggttctgcag 60 97

```
<210> 65
      <211> 377
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(377)
      <223> n = A,T,C or G
      <400> 65
acaacaanaa ntcccttctt taggccactg atggaaacct ggaaccccct tttgatggca
                                                                        60
gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc
                                                                       120
ccaaccetgg tetacecaca nttetggeta tgggetgtet etgccactga acatcagggt
                                                                       180
toggtoataa natgaaatoo caanggggac agaggtoagt agaggaagot caatgagaaa
                                                                       240
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg
                                                                       300
tgggggtgaa ctacccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag
                                                                       360
gggcgggagg agcatgt
                                                                       377
      <210> 66
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 66
acgeettiee eteagaatie agggaagaga etgiegeeig eetteeteeg tigitgegig
agaacccgtg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg
aggaactaac tgcaccetgg tecteteece agtececagt teacceteca teceteacet
                                                                       180
tectecacte taagggatat caacactgee cageacaggg gecetgaatt tatgtggttt
                                                                       240
ttatatattt tttaataaga tgcactttat gtcattttt aataaagtct gaagaattac
                                                                       300
tgttt
                                                                       305
      <210> 67
      <211> 385
      <212> DNA
      <213> Homo sapien
      <400> 67
actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga
ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc
                                                                       120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc
                                                                       180
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg
                                                                       240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg
ceteteccag ggeeccagee tggeeacace tgettacagg geacteteag atgeecatae
                                                                       360
catagittet gigetagigg accgi
                                                                       385
      <210> 68
      <211> 73
      <212> DNA
      <213> Homo sapien
      <400> 68
acttaaccag atatatttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa
                                                                        60
gtttttttaa tgg
                                                                        73 .
```

```
<210> 69
      <211> 536
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(536)
      \langle 223 \rangle n = A,T,C or G
      <400> 69
actagtccag tgtggtggaa ttccattgtg ttgggggctc tcaccctcct ctcctgcagc
                                                                         60
tecagetttg tgetetgeet etgaggagae catggeecag catetgagta ceetgetget
                                                                        120
cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat
                                                                        180
cccgggtggc atctataacg cagaceteaa tgatgagtgg gtacagegtg cccttcactt
                                                                        240
cgccatcage gagtataaca aggccaccaa agatgactae tacagacgte egetgegggt
                                                                        300
actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg
                                                                        360
regaaceata tgtaceaagt eecageeeaa ettggacaee tgtgeettee atgaacagee
                                                                        420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca
                                                                        480
gaangtccct gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc
                                                                        536
      <210> 70
      <211> 477
      <212> DNA
      <213> Homo sapien
     <400> 70
atgaceceta acaggggeee teteageeet eetaatgace teeggeetag ceatgtgatt
                                                                        60
teactteeae tecataaege teeteataet aggeetaeta accaacaca taaccatata
                                                                        120
ccaatgatgg cgcgatgtaa cacgagaaag cacataccaa ggccaccaca caccacctgt
                                                                       180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc
                                                                       240
agggattttt ctgagccttt taccactcca gcctagcccc taccccccaa ctaggagggc
                                                                       300
actggccccc aacaggcatc accocgctaa atcccctaga agtcocactc ctaaacacat
                                                                       360
ocgtattact egcatcagga gtatcaatca cctgagctca ecatagteta atagaaaaca
                                                                       420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt
      <210> 71
      <211> 533
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(533)
      <223> n = A,T,C or G
      <400> 71
agagetatag gtacagtgtg ateteagett tgcaaacaca ttttetacat agatagtact
                                                                        60
aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattggtta
                                                                       120
tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat
                                                                       180
attatttoca taacttaaaa agtgagtttg aaaaagaaaa totocagcaa gcatctcatt
                                                                       240
taaataaagg tttgtcatct ttaaaaaatac agcaatatgt gactttttaa aaaagctgtc
                                                                       300
aaataggtgt gaccctacta ataattatta gaaatacatt taaaaaacatc gagtacctca
                                                                       360
agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg
                                                                       420
cttcgtaatt ttggagtang aggttccctc ctcaattttg tattttaaa aagtacatgg
                                                                       480
taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc
                                                                       533
```

```
<210> 72
      <211> 511
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(511)
      \langle 223 \rangle n = A,T,C or G
      <400> 72
tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta
                                                                      60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa
                                                                     120
aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga
                                                                     180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt
                                                                     240
gaggttetet gtgtgcccac tggtttgaaa accgttetne aataatgata gaatagtaca
                                                                     300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac
                                                                     360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctgttatg
                                                                    420
atttctctcc attgcagcna naaacccgtt cttctaagca aacncaggtg atgatggcna
                                                                     480
aaatacaccc cctcttgaag naccnggagg a
                                                                     511
      <210> 73
      <211> 499
      <212> DNA
     <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1)...(499)
      <223> n = A,T,C or G
     <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac
                                                                      60
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc
                                                                     120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta
                                                                     180
caagtgagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc agggtgcatc
                                                                     240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca
                                                                     300
360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc
                                                                     420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact
                                                                     480
gtcctttcct aantaaaat
                                                                     499
     <210> 74
     <211> 537
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(537)
     <223> n = A,T,C or G
     <400> 74
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat
```

```
ttatcagett aacteagata aaateattga aagtaataag gtaaaageta gtetetaact
                                                                        120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa
                                                                        180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga
                                                                        240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag
                                                                        300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc
                                                                        360
cagtitigett gatatattig tigatattaa gattetigae tiatattiig aatgggttet
                                                                        420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat
                                                                        480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt
                                                                        537
      <210> 75
      <211> 467
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(467)
      \langle 223 \rangle n = A,T,C or G
      <400> 75
caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc
                                                                         60
tgcatattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca
                                                                        120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg
                                                                        180
tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga
                                                                        240
totagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta
                                                                        300
tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa
                                                                        360
caatgaggaa tagccaeggt gatetecage accaaatete tecatgttnt tecagagete
                                                                        420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn
                                                                        467
      <210> 76
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (400)
      <223> n = A,T,C or G
      <400> 76
aagctgacag cattegggee gagatgtete geteegtgge ettagetgtg etegegetae
                                                                         60
tctctctttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgtc
                                                                        120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat
                                                                        180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag
                                                                       240
acttgtcttt cagcaaggac tggtctttct atctcttgta ctacactgaa ttcacccca
                                                                       3-0-0
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng
                                                                       360
ttnagtggga tcganacatg taagcagcan catgggaggt
                                                                       400
      <210> 77
      <211> 248
      <212> DNA
      <213> Homo sapien
      <4.00> 77
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct
```

```
ecagetgeec eggegggga tgegaggete ggageaceet tgeeeggetg tgattgetge
                                                                        120
cagging teateteage tittetgice cittgetece ggcaageget tetgetgaaa
                                                                        180
gttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa
                                                                        240
aaaaaaa
                                                                        248
       <210> 78
       <211> 201
       <212> DNA
      <213> Homo sapien
      <400> 78
actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
                                                                         60
tcacccagac cccgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac
                                                                        120
totgotacto ggaaactatt tttatgtaat taatgtatgo tttottgttt ataaatgoot
                                                                        180
gatttaaaaa aaaaaaaaa a
                                                                        201
      <210> 79
      <211> 552
      <212> DNA
      <213> Homo sapien
      <220'>
      <221> misc feature
      <222> (1) ... (552)
      \langle 223 \rangle n = A, I, C or G
      <40.0> 79
tecttttgtt aggtttttga gacaacceta gacetaaact gtgtcacaga ettetgaatg
                                                                         60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt
                                                                        120
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag
                                                                        180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt
                                                                        240
atgcaagtta gtaattactc agggttaact aaattacttt aatatgctgt tgaacctact
                                                                        300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga
                                                                        360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta
                                                                        420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac
                                                                        480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa
                                                                        540
aaaaaaaaa aa
                                                                        552
      <210> 80
      <211> 476
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(476)
      <223> n = A,T,C or G
      <400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga
                                                                         60
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct
                                                                        120
cacacagact cocgagtage tgggactaca ggcacacagt cactgaagca ggccctgttt
                                                                        180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta
                                                                       240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac
                                                                        300
tettetaagt cetettecag ceteactitg agreetecti gggggttgat aggaaninte
                                                                        360
```

```
tcttggcttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat
                                                                        420
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa
                                                                        476
      <210> 81
      <211> 232
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(232)
      <223> n = A,T,C or G
      <400> 81
tttttttttg tatgeenten etgtggngtt attgttgetg ceaccetgga ggageecagt
                                                                        60
ttettetgta tetttettt etgggggate tteetggete tgececteca tteecageet
                                                                       120
ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcctggtag ccctcagag
                                                                       180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct
                                                                       232
      <210> 82
      <211> 383
      <212> DNA
     <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A,T,C or G
      <400> 82
aggogggago agaagotaaa gocaaagooo aagaagagtg goagtgooag cactggtgoo
                                                                        60
agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtggc ttcagtgctg
                                                                       120
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg
                                                                       180
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt
                                                                       240
gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac
                                                                       300
agcactcing gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg
                                                                       360
ccatttcaaa aaaaaaaaaa aaa
                                                                       383
      <210> 83
      <211> 494
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(494)
      <223> n = A,T,C or G
      <400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca
                                                                        46-0
gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc
                                                                       120
ccatectget eggttetece cagatgacaa atactetega caeegaatea ecateaagaa
                                                                       180
acgetteaag gtgeteatga ceeageaace gegeeetgte etetgagggt cettaaactg
                                                                       240
atgtetttte tgecacetgt tacceetegg agacteegta accaaactet teggactgtg
                                                                       0°0°E
agreetgatg cetttttgcc agreatacte tttggentee agtetetegt ggegattgat
                                                                       3€0
```

```
tatgcttgtg tgaggcaatc atggtggcat cacccatnaa gggaacacat ttgantttt
tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta
                                                                        480
aaaaaaaaa aaaa
                                                                        494
      <210> 84
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(380)
      <223> n = A,T,C or G
      <400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca
                                                                         60
agtatectge geogegiett ctacegiece tacetgeaga tettegggea gattececag
                                                                        120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg
                                                                        180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctggtg
                                                                        240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg
                                                                        300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc
                                                                       360
agcgttnccg cctcatccgg
                                                                        380
      <210> 85
      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(481)
      <223> n = A,T,C or G
      <400> 85
gagttagete etceacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                        60
tnccatcgtc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca
                                                                       120
ggaaactete aatcaagtea cegtenatna aacetgtgge tggttetgte tteegetegg
                                                                       180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga
                                                                       240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc
                                                                       300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac
                                                                       360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa
                                                                       420
aaagaacacc teetggaagt getngeeget eetegteent tggtggnnge gentneettt
                                                                       480
                                                                       481
      <210> 86
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(472)
      <223> n = A,T,C or G
      <400> 86
```

```
aacatettee tgtataatge tgtgtaatat egateegatn ttgtetgetg agaatteatt
acttggaaaa gcaacttnaa gcctggacac tggtattaaa attcacaata tgcaacactt
                                                                                                                                                     120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg
                                                                                                                                                     180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct tttttttga
                                                                                                                                                    240
cacaagteeg aaaaaageaa aagtaaacag tinttaatit gitagocaat teaetiteti
                                                                                                                                                     300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg
                                                                                                                                                     360
atatntgage ggaagantag cettectact teaccagaca caactecttt catattggga
                                                                                                                                                    420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg
                                                                                                                                                    472
             <210> 87
             <211> 413
             <212> DNA
             <213> Homo sapien
            <220>
            <221> misc_feature
            <222> (1)...(413)
            \langle 223 \rangle n = A,T,C or G
            <400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                                                                                                    120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                                                                                                    180
figicition to take the state of the state of
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg
                                                                                                                                                    3.00
ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa
                                                                                                                                                    360
acagaaattg ggtngtatat tgaaananng catcattnaa acgtttttt ttt
            <210> 88
            <211> 448
            <212> DNA
            <213> Homo sapien
            <220>
            <221> misc_feature
            <222> (1) ... (448)
            <223> n = A, T, C or G
            <400> 88
egeagegggt cetetetate tagetecage etetegeetg coccaetece «egeqteceqe
gtoctageon accategoog geocotegog egococegote etcotegoteg ecatectego
                                                                                                                                                    120
cgtggccctg gecgtgagcc cegeggeegg etecagteec ggcaageegc egegeetggt
                                                                                                                                                    180
gggaggeeca tggaeeeege gtggaagaag aaggtgtgeg gegtgeaetg gaetttgeeg
                                                                                                                                                    240
teggenanta caacaaacce geaacnactt ttacenagen egegetgeag gttgtgeege
                                                                                                                                                    300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng
                                                                                                                                                    360
tttaccagaa ccnagccaat tngaacaatt necectecat aacageeect tttaaaaaagg
                                                                                                                                                    420
gaancantcc tgntcttttc caaatttt
                                                                                                                                                    448
            <210> 89
            <211> 463
            <212> DNA
            <213> Homo sapien
            <220>
            <221> misc_feature
```

```
<222> (1)...(463)
      <223> n = A,T,C or G
      <400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca
                                                                         60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc
                                                                        120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt
                                                                        180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc
                                                                        240
tttnatgttn agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg
                                                                        300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn
                                                                        360
aattetetee eeatannaaa acceangeee ttggganaat ttgaaaaang gnteettenn
                                                                        420
aattennana antteagntn teatacaaca naaenggane eee
                                                                        463
      <210> 90
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(400)
      <223> n = A,T,C or G
      <400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt
                                                                         60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat
                                                                        120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact
                                                                        180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct
                                                                        240
cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtccct
                                                                        300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa
                                                                        360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca
                                                                        400
      <210> 91
      <211> 480
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(480)
      \langle 223 \rangle n = A,T,C or G
      <400> 91
gageteggat ecaataatet ttgtetgagg geageacaea tatneagtge eatggnaact
                                                                        60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                        120
atgeetettt gaetaeegtg tgeeagtget ggtgattete acacacetee nneegetett
                                                                       180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga
                                                                       240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt
                                                                       300
tgtcaatact aaccegetgg tttgcctcca tcacatttgt gatctgtagc tctggataca
                                                                       360
tetectgaca gtactgaaga acttettett ttgttteaaa agcaactett ggtgeetgtt
                                                                       420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa
                                                                       480
      <210> 92
```

<211> 477 <212> DNA

```
<213> Homo sapien
       <220>
      <221> misc_feature
      <222> (1)...(477)
      <223> n = A, T, C \text{ or } G
      <400> 92
atacagecca nateceacca egaagatgeg ettgttgaet gagaacetga tgeggteact
                                                                         60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt
                                                                         120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt
                                                                        180
taantgcagg aagaggetga ccacctegeg gtecaccagg atgecegact gtgegggace
                                                                        240
tgcagcgaaa ctectegatg gtcatgageg ggaagegaat gangcecagg geettgeeca
                                                                        3-0-0
gaacetteeg cetgttetet ggegteacet geagetgetg cegetnacae teggeetegg
                                                                        360
accageggae aaacggegtt gaacageege accteaegga tgeecantgt gtegegetee
                                                                        420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg
                                                                        477
      <210> 93
      <211> 377
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(377)
      \langle 223 \rangle n = A,T,C or G
      <400> 93
gaacggctgg accttgcctc gcattgtgct gctggcagga ataccttggc aagcagctcc
                                                                         60
agtecgagea gecceagace getgeegeee gaagetaage etgeetetgg eetteeete
                                                                        120
cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn
                                                                        180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaat ttccaaacaa
                                                                        240
caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta
                                                                        300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa
                                                                        360
ataaatatat tattaaa
                                                                        377
      <210> 94
      <211> 495
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(495)
      <223> n = A, T, C or G
      <400> 94
ccctttgagg ggttagggtc cagttcccag tggaagaaac aggccaggag aantgcgtgc
                                                                         60
cgagctgang cagatttecc acagtgaeec cagageectg ggctatagte tetgaeecet
                                                                        120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg
                                                                        180
gaaggcocca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgccccc
                                                                        240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa
                                                                        300
tgcaagetea ecaaggteee eteteagtee ettecetaca eeetgaaegg neaetggoee
                                                                        360
acacccaccc agancancca occgecatgg ggaatgtnet caaggaateg engggcaacg
                                                                        420
tggactctng tecennaagg gggcagaate tecaatagan gganngaace ettgetnana
                                                                        480
```

```
aaaaaaana aaaaa
                                                                         495
      <210> 95
       <211> 472
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(472)
      <223> n = A,T,C or G
     <400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                         60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt
                                                                        120
tagctgtttt gagttgattc gcaccactgc accacactc aatatgaaaa ctatttnact
                                                                        180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt
                                                                        240
atgatgaaaa gcaatagata tatattettt tattatgttn aattatgatt gccattatta
                                                                        300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac
                                                                        360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata
                                                                        420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at
                                                                        472
      <210> 96
      <211> 476
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (476)
      \langle 223 \rangle n = A,T,C or G
      <400> 96
ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat
                                                                         60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt
                                                                        120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt
                                                                        180
attetteaca gragatgatg aaagagteet ceagtgtett gngcanaatg ttetagntat
                                                                        240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat
                                                                        300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct
                                                                        360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt
                                                                        420
tacaaagtet atetteetea nangtetgtn aaggaacaat ttaatettet agettt
                                                                        476
      <210> 97
      <211> 479
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ...(479)
      <223> n = A,T,C or G
      <400> 97
actetteeta atgetgatat gatettgagt ataagaatge atatgteact agaatggata
                                                                        60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatgaa acacagctta
                                                                        120
```

```
caatcgcaaa tcaaaactca caagtgctca tctgttgtag atttagtgta ataagactta
                                                                        180
gattgtgctc cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat
                                                                        240
caggetacta gaattetgtt attggatatn tgagageatg aaatttttaa naatacaett
                                                                        300
gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat
                                                                        360
ntnnttttta natcaaagta ttttgtgttt ggaantgtnn aaatgaaatc tgaatgtggg
                                                                        420
ttenatetta ttttttecen gaenactant tnetttttta gggnetatte tganecate
                                                                        479
      <210> 98
      <211> 461
      <212> DNA
      <213> Homo sapien
      <400> 98
agtgacttgt cetecaacaa aacceettga teaagtttgt ggcactgaca atcagaceta
                                                                         60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
                                                                        120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                        180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                        240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat
                                                                        300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaaggact
                                                                        360
ttaagaaaaa ctaccacatg ttgtgtatcc tggtgccggc cgtttatgaa ctgaccaccc
                                                                        420
tttggaataa tcttgacgct cctgaacttg ctcctctgcg a
                                                                        461
      <210> 99
      <211> 171
      <212> DNA
      <213> Homo sapien
      <400> 99
gtggccgcgc gcaggtgttt cctcgtaccg cagggccccc tcccttcccc aggcgtccct
                                                                        60
cggcgcctct gcgggcccga ggaggagcgg ctggcgggtg gggggagtgt gacccaccct
                                                                       120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c
                                                                       171
      <210> 100
     <211> 269
      <212> DNA
      <213> Homo sapien
      <400> 100
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc
                                                                        60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc
                                                                       120
aaggetgage tgaegeegea gaggtegtgt caegteecae gaeettgaeg eegtegggga
                                                                       180
cagceggaac agageeeggt gaagegggag geetegggga geeeeteggg aagggeggee
                                                                       240
cgagagatac gcaggtgcag gtggccgcc
                                                                       <del>2</del>69
      <210> 101
      <211> 405
      <212> DNA
      <213> Homo sapien
      <400× 101
ttttttttt ttttggaate tactgegage acageaggte ageaacaagt teattttgea
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                       120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaacgaagca aataacatgg
                                                                       180
agtgggtgca cectecetgt agaacetggt tacaaagett ggggcagttc acetggtetg
                                                                       240
tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatatctttt agagagtcca
                                                                       300
```

```
ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttg
gatgatcagt acgaataccg aggcatattc tcatatcggt ggcca
      <210> 102
      <211> 470
      <212> DNA
      <213> Homo sapien
      <400> 102
60
ggcacttaat ccatttttat ttcaaaatgt ctacaaattt aatcccatta tacggtattt
                                                                     120
tcaaaatcta aattattcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa
                                                                     180
atatacttct ttcagcaaac ttgttacata aattaaaaaa atatatacgg ctggtgtttt
                                                                     240
caaagtacaa ttatcttaac actgcaaaca ttttaaggaa ctaaaataaa aaaaaacact
                                                                     300
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200 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr 215 220 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp 230 235 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val 245 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg 265 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly 280 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly 295 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp 310 <210> 113 <211> 553 <212> PRT <213> Homo sapien <400> 113 Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala Gln Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu 25 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Glu Val Gly Val 40 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly 55 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile 90 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu 105 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly 120 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu 135 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala 150 155 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr 165 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu 185 Gly Thr Gln Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu 200 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly 215 220 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His 230 235 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu 250 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg

265 270 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe 280 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val 295 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly 310 315 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu 325 330 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg 345 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala 355 360 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu 375 ... 380 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala 390 395 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly 405 410 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu 420 425 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala 440 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser 455 460 Ala Cys Asp Val Ser Val Arg Val Val Gly Glu Pro Thr Glu Ala 470 475 Arg Val Vai Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp 485 490 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser 505 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala -525 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp 535 Lys Ser Asp Leu Ala Lys Tyr Ser Ala 545

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

 Met
 Gln
 Cys
 Phe
 Ser
 Phe
 Ile
 Lys
 Thr
 Met
 Met
 Ile
 Leu
 Phe
 Asn
 Leu

 1
 5
 10
 10
 15
 15
 15
 15

 Leu
 Ile
 Phe
 Leu
 Cys
 Gly
 Ala
 Ala
 Ala
 Leu
 Leu
 Leu
 Ala
 Val
 Phe
 Ala
 Ala
 Leu
 Ile
 Phe
 Gly
 Phe
 Ala
 Ala
 Ala
 Gly
 Tyr
 Phe
 Leu
 Ile
 Ala
 Ala
 Lys
 Thr
 Thr
 Tyr
 Phe
 Leu
 Ile
 Lys
 Thr
 Thr
 Tyr
 Ile
 Ile
 Lys
 Ile

```
85 -
                                     90
Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr
                                  105
                                                     110
  Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
                              120
  Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
                          135
  Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
                      150
                                       .. 155
  Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
                  165
                                     170
  Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
              180
                                 185
  His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
                             200
  Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
                          215
                                             220
  Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
  225
                      230
                                         235
  Gln
        <210> 115
        <211> 366
        <212> DNA
        <213> Homo sapien.
        <400> 115
  gctctttctc tcccctcctc tgaatttaat tctttcaact tgcaatttgc aaggattaca
  120
  ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                      180
  actggtagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                      240
  tctcagaacc atttcaccca gacagcctgt ttctatcctg tttaataaat tagtttgggt
                                                                      300
  tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt
                                                                      360
  ttagtc
                                                                      366
        <210> 116
        <211> 282
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1)...(282)
        <223> n = A,T,C or G
        <400> 116
  acaaagatga accattteet atattatage aaaattaaaa tetaceegta ttetaatatt
                                                                       60
  gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa
                                                                      120
  agactttact attttcatat tttaagacac atgatttatc ctattttagt aacctggttc
                                                                      180
  atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt
                                                                      240
  tcaatcinga actaictana tcacagacat tictaticci ti
                                                                      282
```

<210> 117 <211> 305

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<212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(305)
      \langle 223 \rangle n = A,T,C or G
      <400> 117
acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca
                                                                          60
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa
                                                                         120
aataaggcaa aatatatgaa acaacaggto togagatatt ggaaatcagt caatgaagga
                                                                         180
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt
                                                                         240
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat
                                                                         300
tgggt
                                                                         305
      <210> 118
      <211> 71
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(71)
      <223> n = A,T,C or G
      <400> 118
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa
                                                                          60
aantcctggg t
                                                                          71
      <210> 119
      <211> 212
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (212)
      <223> n = A,T,C or G
      <400> 119
actocggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca
                                                                         60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac
                                                                        120
agtaagetgg ceettetaat aaaagaaaat tgaaaggttt eteactaane ggaattaant
                                                                        180
aatggantca aganactccc aggcctcagc gt
                                                                        212
      <210> 120
      <211> 90
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (90)
      <223> n = A,T,C or G
```

```
<400> 120
actogttgca natcaggggc cocccagagt caccgttgca ggagtccttc tggtcttgcc
                                                                         60
ctccgccggc gcagaacatg ctggggtggt
                                                                        .. 90.
      <210> 121
      <211> 218
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(218)
      <223> n = A,T,C or G
      <400> 121
tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga
                                                                         60
gaataagatt tgctaaaaga tttggggcta aaacatggtt attgggagac atttctgaag
                                                                        120
atatnoangt aaattangga atgaattoat ggttottttg ggaattoott tacgatngco
                                                                        180
agcatanact tcatgtgggg atancagcta cccttgta
                                                                        218
      <210> 122
      <211> 171
      <212> DNA
      <213> Homo sapien
      <400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg
                                                                         60
catttgttag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt
                                                                        120
caccaccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t
                                                                        171
      <210> 123
      <211> 76
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1)...(76)
      <223> n = A,T,C or G
      <400> 123
tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca
                                                                         60
ttatcaanta ttgtgt
                                                                         76
      <210> 124
      <211> 131
      <212> DNA
      <213> Homo sapien
      <400> 124
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt
                                                                        60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg
                                                                       120
ttaagatttg t
                                                                       131
```

```
<210> 125
      <211> 432
      <212> DNA
      <213> Homo sapien
      <400> 125
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg
                                                                         60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa
                                                                        120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat
                                                                        180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg
                                                                        240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc
                                                                        300
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaatctcag
                                                                        360
caggaaacat cagaaccact atttctagc cctctgtcag agcaaacctc agtgcctctc
                                                                        420
ctctttgctt gt
                                                                        432
      <210> 126
      <211> 112
      <212> DNA
      <213> Homo sapien
      <400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt qt
                                                                        112
      <210> 127
      <211> 54
      <212> DNA
      <213> Homo sapien
      <400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaagcaca gcag
      <210> 128
      <211> 323
      <212> DNA
      <213> Homo sapien
      <400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagete
                                                                        60
acctgagata acagaatgaa aatggaagga cagccagatt teteetttge tetetgetea
                                                                       120
ttctctctga agtctaggtt acccattttg gggacccatt ataggcaata aacacagttc
                                                                       180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt
                                                                       240
ttcctgcaaa aggctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct
                                                                       300
aggctgcctt cttttccatg tcc
                                                                       323
      <210> 129
      <211> 192
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(192)
      <223> n = A, T, C or G
```

```
<400> 129
acatacatgt gtgtatattt ttaaatatca cttttgtatc actctgactt tttagcatac
                                                                         60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc
                                                                        120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg
                                                                        180
gataaacaaa gt
                                                                        192
      <210> 130
      <211> 362
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(362)
      <223> n = A, T, C or G
      <400> 130
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca
                                                                         60
tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa
                                                                        120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa
                                                                       180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata
                                                                        240
cttatttaaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat
                                                                        300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaatctta aaaagtaatg
                                                                        360
gg
                                                                        362
      <210> 131
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (332)
      <223> n = A,T,C or G
      <400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga
                                                                       120.
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc
                                                                       180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa
                                                                       240
cttccatctg ttatcactgg agaaagecca gacteeccan gaenggtaeg gattgtggge
                                                                       300
atanaaggat tgggtgaagc tggcgttgtg gt
                                                                       332
      <210> 132
      <211> 322
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(322)
      <223> n = A, T, C or G
      <400> 132
actitigcca titigtatat ataaacaatc tigggacatt ciccigaaaa ciaggigtcc
```

```
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct
                                                                         300
gtaacaatct acaattggtc ca
                                                                         322
      <210> 133
      <211> 278
      <212> DNA
      <213> Homo sapien
      <22.0>
      <221> misc_feature
      <222> (1)...(278)
      \langle 223 \rangle n = A,T,C or G
      <400> 133
acaagcette acaagtttaa etaaattggg attaatettt etgtanttat etgeataatt
                                                                          60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta
                                                                         120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctq
                                                                         180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt
                                                                         240
cccacgaaac actaataaaa accacagaga ccagcctq
                                                                         278
      <210> 134
      <211> 121
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(121)
      <223> n = A,T,C or G
      <400> 134
gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta ttttaaaaca
tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg
                                                                        120
                                                                         121
      <210> 135
      <211> 350
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(350)
      \langle 223 \rangle n = A,T,C or G
      <400> 135
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc
                                                                         60
atancaagtg gtgactggtt aagcgtgega caaaggtcag ctggcacatt acttgtgtgc
                                                                        120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca
                                                                        180
gggtgccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct
                                                                        240
ccacctcaat caageeetgg gecatgetac etgeaattgg etgaacaaac gtttgetgag
                                                                        300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt
                                                                        350
```

```
<210> 136
      <211> 399
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(399)
      <223> n = A,T,C or G
      <400> 136
tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt
                                                                         60
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct
                                                                        120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga
                                                                        180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag
                                                                        240
aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc
                                                                        300
tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg
                                                                        360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt
                                                                        399
      <210> 137
      <211> 165
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(165)
      \langle 223 \rangle n = A,T,C or G
      <400> 137
actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt
                                                                        60
ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga
                                                                        120
ttggctggtc ccactggtgg tcactgtcat tggtggggtt cctgt
      <210> 138
      <211> 338
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(338)
      <223> n = A,T,C or G
     <400> 138
actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc
                                                                        60
ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa
tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg
                                                                        180
tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt
                                                                       240
cangectcag gaagectcaa gttecattca getttgecae tgtacattce ccatntttaa
                                                                       300
aaaaactgat gcctttttt ttttttttg taaaattc
                                                                       338
      <210> 139
      <211> 382
```

```
<212> DNA
      <213> Homo sapien
      <400> 139
gggaatettg gtttttggca tetggtttge etatageega ggceaetttg acagaacaaa
                                                                         60
gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga
                                                                        120
attcaaacag acctegteat teetggtgtg ageetggteg geteacegee tateatetge
                                                                        180
atttgcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg
                                                                        240
cettatttgt ettetacace ceacagggee ecetacttet teggatgtgt ttttaataat
                                                                        300
gtcagctatg tgccccatcc tecttcatgc cetecetece tttcctacca etgctgagtg
                                                                        360
gcctggaact tgtttaaagt gt
                                                                        382
      <210> 140
      <211> 200
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(200)
      \langle 223 \rangle n = A,T,C or G
      <400> 140
accaaanctt ctffctgttg tgttngattt tactataggg gtttngcttn ttctaaanat
                                                                         60
actiticati taacanciit igitaagigi caggoigcac tiigciccat anaattatig
                                                                        120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt
                                                                        180
atattcagca taaaggaqaa
                                                                        200
      <210> 141
      <211> 335
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(335)
      <223> n = A,T,C or G
      <400> 141
actitatiti caaaacactc atatgitgca aaaaacacat agaaaaataa agiitggigg
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggttgtt
                                                                        120
atgcatgtag agaacccaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga
                                                                        180
aatggttetg agaaccatee aatteacetg teagatgetg atanactage tetteagatg
                                                                       240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg
                                                                        300
attcacaaac caagtaattt taaacaaaga cactt
                                                                        335
      <210> 142
      <211> 459
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(459)
      <223> n = A,T,C or G
```

```
<400> 142
accaggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta
                                                                        60
gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat
                                                                       120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca
                                                                       180
cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc
                                                                       240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca
                                                                       300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga
                                                                       360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct
                                                                       420
cagcangggt gggaggaacc agctcaacct tggcgtant
                                                                       459
      <210> 143
      <211> 140
      <212> DNA
      <213> Homo sapien
      <400> 143
acattteett ecaccaagte aggacteetg gettetgtgg gagttettat cacctgaggg
                                                                        60
aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag
                                                                       120
accatccgac ttccctgtgt
                                                                       140
      <210> 144
      <211> 164
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (164)
      <223> n = A,T,C or G
      <400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct
                                                                        60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg
                                                                       120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt
                                                                       164
      <210> 145
      <211> 303
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(303)
      <223> n = A,T,C or G
      <400> 145
acgtagacca tecaactttg tatttgtaat ggcaaacate cagnagcaat tectaaacaa
                                                                       60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat
                                                                       120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca
                                                                       180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag
                                                                       240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat
                                                                       300
caa
                                                                       303
```

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<211> 327
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(327)
      <223> n = A,T,C or G
      <400> 146
actgcagctc aattagaagt ggtctctgac tttcatcanc ttctcoctgg gctccatgac
                                                                         60
actggcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct
                                                                        120
ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt
                                                                        180
cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc
                                                                        240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg
                                                                        300
taggggtgag ctgtgtgact ctatggt
                                                                        327
      <210> 147
      <211> 173
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(173)
      <223> n = A,T,C or G
      <400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg
                                                                        60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                        120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt
                                                                        173
      <210> 148
      <211> 477
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(477)
      <223> n = A, T, C or G
      <400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct
                                                                        60
atgggatata ttatttgatg ctecatttca tcacacatat atgaataata cactcatact
                                                                       120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg
                                                                       180
gtggtcctag tggccatcag tccangectg cacettgage cettgagete cattgctcae
                                                                       240
nccancecac ctcaccgacc ccatcetett acacagetac ctcettgete tetaacceca
                                                                       300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag
                                                                       360
caccactggt aagcettete cagecaacae acacacaea acacneacae acacacatat
                                                                       420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg
                                                                       477
      <210> 149
      <211> 207
      <212> DNA
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# <213> Homo sapien <400> 149 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60 taacgtattt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct 120 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180 tttcaggcag agggaacagc agtgaaa 207 <210> 150 <211> 111 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(111) <223> n = A,T,C or G<400> 150 accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60 cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111 <210> 151 <211> 196 <212> DNA <213> Homo sapien <400> 151 agcgcggcag gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac 60 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120 ggataccaac cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag 180 gtgcatccgg ctcagt 196 <210> 152 <211> 132 <212> DNA <213> Homo sapien <400> 152 acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagaac 60 cttccccttt tcatctagtg gtggaaacct gatgctttat gttgacagga atagaaccag 120 gagggagttt gt 132 <210> 153 <211> 285 <212> DNA <213> Homo sapien <220> <221> misc\_feature <222> (1) ... (285) $\langle 223 \rangle$ n = A,T,C or G <400> 153 acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag

```
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga
                                                                        120
gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac
                                                                        18Ó
cctggctagt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca
                                                                        240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt
                                                                        285
      <210> 154
      <211> 333
      <212> DNA
      <213> Homo sapien
      <400> 154
accacagtee tgttgggeea gggetteatg accettetg tgaaaageea tattateace
                                                                         60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac
                                                                        120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg
                                                                        180
attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctgatttg
                                                                        240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg
                                                                        300
gtcaggcctg tctcatccat atggatcttc cgg
                                                                        333
      <210> 155
      <211> 308
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(308)
      <223> n = A, T, C \text{ or } G
      <400> 155
actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg
gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat
                                                                        120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag ccccagccc
                                                                       180
atcacagete actgetetgt teatecagge ecageatgta gtggetgatt ettettgget
                                                                       240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg
                                                                       300
gccctggt
                                                                       308
    <210> 156
      <211> 295
      <212> DNA
      <213> Homo sapien
      <400> 156
accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta
                                                                        60
ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga
                                                                       120
gaataggaga ttatgtttgg coctcatatt ctctcctatc ctccttgcct cattctatgt
                                                                       180
ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat
                                                                       240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat
                                                                       295
      <210> 157
      <211> 126
      <212> DNA
      <213> Homo sapien
      <400> 157
acaagtttaa atagtgetgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct
```

```
gaagagcaaa acaaattetg teatgtaate tetatettgg gtegtgggta tatetgteee
                                                                        120
cttagt
                                                                        126
      <210> 158
      <211> 442
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(442)
      <223> n = A,T,C or G
      <400> 158
acceactggt cttggaaaca cccatcetta atacgatgat ttttctgtcg tgtgaaaatg
                                                                         60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt
                                                                        120
gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt
                                                                        180
ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta
                                                                        240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggtg
                                                                        300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga
                                                                        360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg
                                                                        420
tgttcattct ctgatgtcct gt
                                                                        442
      <210> 159
      <211> 498
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(498)
     <223> n = A,T,C or G
      <400> 159
acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc
                                                                        60
tccaacaaga actgaggttg cagagcgggt agggaagagt gctgttccag ttgcacctgg
                                                                       120
gctgctgtgg actgttgttg attcctcact acggcccaag gttgtggaac tggcanaaag
                                                                       180
gtgtgttgtt gganttgagc tcgggcggct gtggtaggtt gtgggctctt caacaggggc
                                                                       240
tgctgtggtg ccgggangtg aangtgttgt gtcacttgag cttggccagc tctggaaagt
                                                                       300
antanattet teetgaagge cagegettgt ggagetggea ngggteantg ttgtgtgtaa
                                                                       360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn
                                                                       420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc
                                                                       480
aagggaataa gctgtggt
                                                                       498
      <210> 160
      <211> 380-
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (380)
      <223> n = A, T, C or G
      <400> 160
```

```
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac
                                                                         60
agetteagga taetteeagg agacagagee accageagea aaacaaatat teecatgeet
                                                                        120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc
                                                                        180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc
                                                                        240
ccaccettae etceatetea cacacttgag etttecacte tgtataatte taacateetg
                                                                       300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa
                                                                       360
cttgtagaat gaagcctgga
                                                                        380
      <210> 161
      <211> 114
      <212> DNA
      <213> Homo sapien
      <400> 161
actecacate ecetetgage aggeggttgt egtteaaggt gtatttggee ttgeetgtea
                                                                        60
cactgtecac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt
                                                                       114
      <210> 162
      <211> 177
      <212> DNA
      <213> Homo sapien
      <400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa
                                                                        60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt
                                                                       120
tggtgatata taacttggca ataacccagt ctggtgatac ataaaactac tcactgt
                                                                       177
      <210> 163
      <211> 137
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (137)
      <223> n = A,T,C or G
      <400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac
                                                                        60
canagaagge agetacgget actectacat cetggegtgg gtggeetteg eetgcaeett
                                                                       120
catcagcggc atgatgt
                                                                       137
      <210> 164
      <211> 469
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1)...(469)
      <223> n = A,T,C or G
      <400> 164
cttatcacaa tgaatgttet eetgggcage gttgtgatet ttgecacett egtgacttta
                                                                        60
tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaocaggaaa
                                                                       120
```

```
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt
                                                                        180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg
                                                                        240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg
                                                                        300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct
                                                                        360
tctagtaggc acagggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat
                                                                        420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt
                                                                       469
      <210> 165
      <211> 195
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(195)
      <223> n = A,T,C or G
      <400> 165
acagtttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctggtgg
                                                                        60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc
                                                                       120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact
                                                                       180
tcctctgaga tgagt
                                                                       195
      <210> 166
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A,T,C or G
      <400> 166
acatettagt agtgtggeae atcaggggge cateagggte acagteaete atageetege
                                                                        60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct
                                                                       120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt
                                                                       180
tttgcagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcaggtg
                                                                       240
gatgecaace tegtetangg teegtgggaa getggtgtee aenteaceta caacetggge
                                                                       300
gangatetta taaagagget eenagataaa etecaegaaa ettetetggg agetgetagt
                                                                       360
nggggccttt ttggtgaact ttc
                                                                       383
      <210> 167
      <211> 247
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc_feature
      <222> (1)...(247)
      <223> n = A,T,C or G
      <400> 167
acagagecag acettggeca taaatgaane agagattaag actaaacece aagteganat
                                                                        60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc
                                                                       120
```

```
tatanccata cacagageca acteteagge caaggenatg gttggggeag anceagagae
                                                                       180
tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac
                                                                       240
tgangtc
                                                                       247
      <210> 168
      <211> 273
      <212> DNA
      <213> Homo sapien
      <220'>
      <221> misc_feature
      <222> (1)...(273)
      <223> n = A,T,C or G
      <400> 168
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa
                                                                        60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg
                                                                       120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc
                                                                       180
aattcccaac ttccttgcca caagettccc aggetttctc ccctggaaaa ctccagettg
                                                                       240
agtcccagat acactcatgg gctgccctgg gca
                                                                       273
      <210> 169
      <211> 431
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (431)
      <223> n = A,T,C or G
      <400> 169
acageettgg ettecceaaa etceacagte teagtgeaga aagateatet tecageagte
                                                                        -60
agctcagacc agggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta
                                                                       120
ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag
                                                                       180
ggcagcagaa agggggtant tactgatgga caccatette tetgtataet ceacactgae
                                                                       240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc
                                                                       3:00
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg
                                                                       360
aaagtgatet gataetggat tettaattae etteaaaage ttetggggge cateagetge
                                                                       420
tcgaacactg a
                                                                       431
      <210> 170
      <211> 266
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(266)
      <223> n = A,T,C or G
      <400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc
                                                                        60
tcaaggaget etgeaggeat tttgecaane etetecanag canagggage aacetacact
                                                                       120
ccccgctaga aagacaccag attggagtcc tgggagggg agttggggtg ggcatttgat
                                                                       180
```

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gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct
                                                                     240
tcaaagctag gggtctggca ggtgga
                                                                     266
      <210> 171
      <211> 1248
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1) ... (1248)
      <223> n = A, T, C or G
      <400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca
                                                                      60
ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg
                                                                     120
tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg
                                                                     180
cacagtettg aggeegacea agageeaggg ageeagatgg tggaggeeag ceteteegta
                                                                     240
cggcacccag agtacaacag accettgete getaacgace teatgeteat caagttggae
                                                                     300
gaateegtgt eegagtetga caccateegg agcateagea ttgettegea gtgeectace
                                                                     360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc
                                                                     420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac
                                                                     480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc
                                                                     540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc
                                                                     600-
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc
                                                                     660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa
                                                                     720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct
                                                                     780
ccctcaggcc caggagtcca ggcccccagc ccctcctccc tcaaaccaag ggtacagatc
                                                                     840
cccagcccct cctccctcag acccaggagt ccagaccccc cagcccctcc tccctcagac
                                                                     900
ccaggagtcc agccctcct ccctcagacc caggagtcca gaccccccag ccctcctcc
                                                                     960
ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc
                                                                    1020
ccaaccente attecceaga cccagaggte caggteccag cecetentee etcagaccea
                                                                    1080
geggtecaat gecaectaga etntecetgt acaeagtgee eeettgtgge aegttgaeee
                                                                    1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt
                                                                    1200-
1248
      <210> 172
      <211> 159
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(159)
      <223> Xaa = Any Amino Acid
      <400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
                                   10
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
                               25
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
    50
                       55
                                           60
```

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Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
                                     90
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
                                 105
                                                     110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
                             120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
                        135
                                             140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
145
                    150
      <210> 173
      <211> 1265
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(1265)
      <223> n = A,T,C or G
      <400> 173
ggcagcccgc actcgcagcc ctggcaggcg gcactggtca tggaaaacga attqttctqc
                                                                        60
tegggegtee tggtgcatee geagtgggtg etgtcageeg cacactgttt ceagaactee
                                                                       120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg
                                                                       180
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac
                                                                       240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc
                                                                       300
attgcttcgc agtgccctac cgcggggaac tcttgcctcg tttctggctg gggtctgctg
                                                                       360
gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg
                                                                       420
cgggggctga cecagagete tgcgtcecag gcagaatgee taccgtgctg cagtgcgtga
                                                                       480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca
                                                                       540
gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg
                                                                       600
ggcccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg
                                                                       660
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga
                                                                       720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac
                                                                       780
atcctgcgga aggaattcag gaatatetgt teccageece tecteectea ggeecaggag
                                                                       840
tecaggeece cageceetee teceteaaac caagggtaca gatececage ecetecteee
                                                                       900
tragacroag gagtroagar ecorragers etectoretr agarcragga gtroagerer
                                                                       960
tecteentea gacceaggag tecagacece ceagcecte etoceteaga cecaggggtt
                                                                      1.020
gaggecceca acceptecte etteagagte agaggtecaa geocceaace ectegtteec
                                                                      1080
cagacccaga ggtnnaggtc ccageccctc ttccntcaga cccagnggtc caatgccacc
                                                                      1140
tagattttcc ctgnacacag tgcccccttg tggnangttg acccaacctt accagttggt
                                                                      1200
ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa
                                                                      1260
aaaaa
                                                                      1265
      <210> 174
      <211> 1459
      <212> DNA
      <213> Homo sapien
```

<220>

<221> misc\_feature <222> (1)...(1459)

### $\langle 223 \rangle$ n = A,T,C or G

### <400> 174

ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggcc 60 tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120 tacggcaccc agagtacaac agacccttgc tcgctaacga cctcatgctc atcaagttgg 180 acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcccta 240 ccgcggggaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg 300 gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct 360 ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga 420 ngaggtetge antaagetet atgaceeget gtaceacee ancatgttet gegeeggegg 480 agggcaagac cagaaggact cctgcaacgt gagagaggg aaaggggagg gcaggcgact 540 cagggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600 atggagagac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa 660 ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720 agaaacacac acacatagaa atgcagttga cettecaaca gcatggggee tgagggeggt 780 gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa 840 atagectact gttgaegggg agecttaeca ataacataaa tagtegattt atgeataegt 900 tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc 960 gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga 1020 aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080 gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140 aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt 1200 gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260 gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320 aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380 gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440 Саааааааа ааааааааа

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(1167)

<223> n = A,T,C or G

## <400> 175

gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60 gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180 ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc 240 aagttggacg aatcegtgte egagtetgae accateegga geateageat tgettegeag 300 tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360 atgectaceg tgetgeactg egtgaacgtg teggtggtgt etgaggangt etgeagtaag 420 ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag 480 gacteetgea aeggtgaete tggggggeee etgatetgea aegggtaett geagggeett 540 gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc 600 tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga 660 acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720 geocetecte ecteaggeee aggagteeag geocetagee cetectect caaaccaagg 780 gtacagatec ecageceete eteceteaga eccaggagte cagacecece ageceetent 840 centeagace caggagteca geceetecte enteagacge aggagtecag acceecage 900

```
cententeeg teagacecag gggtgeagge ecceaacece tenteentea gagteagagg
                                                                       960
tecaageeee caaceeteg treeceagae ceagaggine aggreecage eccrectore
                                                                      1020
tcagacccag cggtccaatg ccacctagan tntccctgta cacagtgccc ccttgtggca
                                                                      1080
ngttgaccca accttaccag ttggtttttc attttttgtc cctttcccct agatccagaa
                                                                      1140
ataaagtnta agagaagcgc aaaaaaa
                                                                      1167
      <210> 176
      <211> 205
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(205)
      <223> Xaa = Any Amino Acid
      <400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
                   70
                                        75
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
                                105
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
                        135
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
                    150
                                        155
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
                165
                                    170
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
                                185
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
        195
                            200
      <210> 177
      <211> 1119.
      <212> DNA
      <213> Homo sapien
      <400> 177
gcgcactcgc agecctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc
                                                                       60
gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc
                                                                      120
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag
                                                                      180
gecageetet cegtaeggea eccagagtae aacagaceet tgetegetaa egaceteatg
                                                                      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct
```

```
tegeagtgee ctacegeggg gaactettge etegtttetg getggggtet getggegaac
                                                                       360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc
                                                                       420
caaccetgge agggttgtac cattteggea actteeagtg caaggacgte etgetgeate
                                                                       480
ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag
                                                                       540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt
                                                                       600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc
                                                                       660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc
                                                                       720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa
                                                                       780
ttcatttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca
                                                                       840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg
                                                                       900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca
                                                                       960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg
                                                                      1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc
                                                                      1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa
                                                                      1119
      <210> 178
      <211> 164
      <212> PRT
      <213> Homo sapien
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<220>
<221> VARIANT
<222> (1)...(164)
<223> Xaa = Any Amino Acid

<400> 178

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Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
                                    10
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                                25
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
                            40
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
                       . 55
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
                                    90
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
                                105
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
                            120
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
                        135
                                            140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
                    150
                                                             160
Pro Gly Thr Leu
```

<210> 179 <211> 250 <212> DNA <213> Homo sapien

<400> 179

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ctggagtgcc ttggtgtttc aagcecetge aggaagcaga atgcaeette tgaggcaeet
                                                                         60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct
                                                                        120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga
                                                                        180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa
                                                                        240
aaaaaaaaa
                                                                        250
      <210> 180
      <211> 202
      <212> DNA
      <213> Homo sapien
      <400> 180
actagtocag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
                                                                         60
tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta
                                                                        120
ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc
                                                                        180
tgatttaaaa aaaaaaaaaa aa
                                                                        202
     <210> 181
      <211> 558
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (558)
      \langle 223 \rangle n = A,T,C or G
      <400> 181
tccytttgkt naggtttkkg agacamecck agacctwaan ctgtgtcaca gacttcyngg
                                                                         60
aatgtttagg cagtgctagt aatttcytcg taatgattct gttattactt tcctnattct
                                                                        120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa
                                                                        180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatocattca
                                                                        240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac
                                                                        300
ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa
                                                                        360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw
                                                                        420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt
                                                                        480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc
                                                                        540
caaaaaaaa aaaaaaaa
                                                                       558
      <210> 182
      <211> 479
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (479)
      <223> n = A,T,C or G
      <400> 182
acagggwttk grggatgeta agsccccrga rwtygtttga tccaaccctg gcttwttttc
                                                                        60
agaggggaaa atggggccta gaagttacag mscatytagy tggtgcgmtg gcacccttgg
                                                                       120
cstcacacag astoccgagt agctgggact acaggcacac agtcactgaa gcaggccctg
                                                                       180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca
                                                                       240
ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca
                                                                       300
```

```
tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant
                                                                        360
ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara
                                                                        420
awtgstgara aaattaaaat gttctggtty mactttaaaa araaaaaaaa aaaaaaaaa
                                                                        479
       <210> 183
       <211> 384
       <212> DNA
      <213> Homo sapien
       <400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc
                                                                        60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtggtgg cttcagtgct
                                                                       120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt
                                                                       180
gccagcacca gtggcagctc tggtgcctgt ggtttctcct acaagtgaga ttttagatat
                                                                       240
tgttaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca
                                                                       300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt
                                                                       360
gccatttcaa aaaaaaaaaa aaaa
                                                                       384
      <210> 184
      <211> 496
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(496)
      <223> n = A,T,C or G
      <400> 184
accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc
                                                                        60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag
                                                                       120
cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga
                                                                       180
aacgetteaa ggtgeteatg acceageaac egegeeetgt eetetgaggg teeettaaac
                                                                       240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact cttcggactg
                                                                       300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg
                                                                       360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt
                                                                       420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst
                                                                       480
taaaaaaaa aaaaaa
                                                                       496
      <210> 185
      <211> 384
      <212> DNA
      <213> Homo sapien
      <400> 185
gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc
                                                                        60
caagtateyt gegesgegte ttetacegte eetacetgea gatetteggg cagatteece
                                                                       120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct
                                                                       180
gggcacaccc tectggggee caggeggea cetgegtete ecagtatgee aactggetgg
                                                                       240
tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aacttgctca
                                                                       300
ttgccatgtt cagttacaca ttcggcaaag tacagggcaa cagcgatctc tactgggaag
                                                                       360
gcgcagcgtt accgcctcat ccgg
                                                                       384
      <210> 186
```

<211> 577

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(577)
      <223> n = A,T,C or G
      <400> 186
gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                        60
tnccategic atactgtagg titgccacca cytectggca tettggggcg gentaatatt
                                                                       120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc
                                                                       180
teggtgtgaa aggatetece agaaggagtg etegatette eccaeaettt tgatgaettt
                                                                       240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac
                                                                       300
cagecetate atgeegttga megtgeegaa gareacegag cettgtgtgg gggkkgaagt
                                                                       360
ctcacocaga ttctgcatta ccagagagec gtggcaaaag acattgacaa actcgcccag
                                                                       420
gtggaaaaag amcameteet ggargtgetn geegeteete gtemgttggt ggeagegetw
                                                                       480
tecttttgae acacaaacaa gttaaaggea ttttcageec ecagaaantt gtcatcatee
                                                                       540
aagatntege acageaetna teeagttggg attaaat
                                                                       577
      <210> 187
      <211> 534
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(534)
      <223> n = A,T,C or G
      <400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw
                                                                        60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact
                                                                       120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta
                                                                       180
tgccctattc acacotgtta aaagggcgct aagcattttt gattcaacat cttttttt
                                                                       240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc
                                                                       300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttygggagc
                                                                       360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg
                                                                       420
ggatgttnac naaagtwatg tototwacag atgggatgct tttgtggcaa ttotgttctg
                                                                       480
aggatetece agtttattta ceaettgeae aagaaggegt tttetteete agge
                                                                       534
      <210> 188
      <211> 761
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(761)
      <223> n = A,T,C or G
      <400> 188
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                        60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                       120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
```

```
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                        240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg
                                                                        300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa
                                                                        360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt
                                                                        420
gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgtttttt tatnataaaa
                                                                        480
cttgcccttc attacatgtt tnaaagtggt gtggtgggcc aaaatattga aatgatggaa
                                                                        540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac
                                                                        600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta
                                                                        660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac
                                                                        720
gaaaataata acattgaaga aaaananaaa aaanaaaaaa a
                                                                       761
      <210> 189
      <211> 482
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(482)
      <223> n = A,T,C or G
      <400> 189
tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca
                                                                        60
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca
                                                                       120
aageegeetg etgeettete tgtetgtete etggtgeagg cacatgggga gacetteece
                                                                       180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag
                                                                       240
tgataggcac aggccacccg gtacagaccc ctcggctcct gacaggtnga tttcgaccag
                                                                       300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc
                                                                       360
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg
                                                                       420
gttcggccca gctccncgtc caaaaantat tcacccnnct ccnaattgct tgcnggnccc
                                                                       480
CC
                                                                       482
      <210> 190
      <211> 471
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(471)
      <223> n = A,T,C or G
      <400> 190
ttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg
                                                                        60
aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca
                                                                       120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag
                                                                       180
cgcttttgac atacaatgca caaaaaaaaa agggggggg gaccacatgg attaaaattt
                                                                       240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt
                                                                       300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtgatcat gantneteta
                                                                       360
ctacatchac cttgatcatt gccaggaach aaaagtthaa ancachchgt acaaaaanaa
                                                                       420
tetgtaattn antteaacet eegtaengaa aaatnttnnt tatacaetee e
                                                                       471
      <210> 191
      <211> 402
```

<212> DNA

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(402)
      <223> n = A, T, C or G
      <400> 191
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct
                                                                         60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa
                                                                        120
attetteace agreacatet tetaggacet tittggatte agrtagtata agetetteca
                                                                        180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg
                                                                        240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc
                                                                        300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc
                                                                        360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca
                                                                        402
      <210> 192
      <211> 601
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(601)
      \langle 223 \rangle n = A,T,C or G
      <400> 192
gageteggat ecaataatet tigietgagg geageacaea taineagige caiggnaaci
                                                                         60
ggtctacccc acatgggagc agcatgccgt agniatataa ggtcattccc tgagtcagac
                                                                        120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatccgyt
                                                                        180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc
                                                                        240
acgagacact tgaaaggtgt aacaaagcga ytettgcatt getttttgte ecteeggeac
                                                                        300
cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga
                                                                        360
tacateteet gacagtactg aagaacttet tetttegttt caaaagcare tettggtgee
                                                                        420
tgttggatca ggttcccatt teccagtcyg aatgttcaca tggcatattt wactteccac
                                                                        4.80
aaaacattgc gatttgaggc tcagcaacag caaatectgt tccggcattg gctgcaagag
                                                                        540
cctcgatgta gecggccagc gecaaggcag gegeegtgag eeccaocagc agcagaagca
                                                                        600
g
                                                                        601
      <210> 193
      <211> 608
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(608)
      <223> n = A, T, C or G
      <400> 193
atacagecca nateccaeca egaagatgeg ettgttgaet gagaacetga tgeggteaet
                                                                        6-0
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt
                                                                        120
cccaacgcag gcagmagegg gsecggtcaa tgaactccay tegtggettg gggtkgaegg
                                                                        1:80
tkaagtgcag gaagaggctg accaeetege ggtecaeeag gatgeeegae tgtgegggae
                                                                       240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc
                                                                       300
```

```
agaacettee geetgttete tggegteace tgeagetget geegetgaea eteggeeteg
                                                                        360
gaccagegga caaaeggert tgaacageeg caceteaegg atgeecagtg tgtegegete
                                                                        420
caggammgsc accagegtgt ccaggtcaat gteggtgaag ceeteegegg gtratggegt
                                                                        480
ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga
                                                                        540
gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaactc
                                                                        600
cacgcaat
                                                                        608
      <210> 194
      <211> 392
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(392)
      <223> n = A,T,C or G
      <400> 194
gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt
                                                                         60
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc
                                                                        120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg
                                                                        180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac
                                                                        240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt
                                                                        300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg
                                                                        360
aaataaatat agttattaaa ggttgtcant cc
                                                                        392
      <210> 195
      <211> 502
      <212> DNA
      <213> Homo sapien
      <220>
      <221'> misc_feature
      <222> (1)...(502)
      \langle 223 \rangle n = A,T,C or G
      <400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg
                                                                         60
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc
                                                                        120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc
                                                                        180
aagggaaggc cccattccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc
                                                                        240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca
                                                                        300
caaatgcaag ctcaccaagg teeectetea gteeecttee stacaceetg ameggeeact
                                                                        360
gscscacacc cacccagage acgccacccg ccatggggar tgtgctcaag gartcgcngg
                                                                        420
gcarcgtgga catcingtcc cagaaggggg cagaatctcc aatagangga cigarcmstt
                                                                        480
gctnanaaaa aaaaanaaaa aa
                                                                        502
      <210> 196
      <211> 665
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (665)
```

#### <223> n = A,T,C or G

```
<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                       60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt
                                                                       120
wagetgtttk gagttgatts geaccactge acceacaact teaatatgaa aacyawttga
                                                                       180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc
                                                                       240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt
                                                                       300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact
                                                                       360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt
                                                                       420
watatttatt teattaattt ettteetkgt ttaegtwaat tttgaaaaga wtgeatgatt
                                                                       480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt
                                                                       540
ttcttagaat gtataaaggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac
                                                                       600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan
                                                                       660
aaqtq
                                                                       665
      <210> 197
      <211> 492
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(492)
      <223> n-= A, T, C or G
      <400> 197
ttttnttttt tttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat
                                                                        60
atgittattg gagcgatcca ttatcagtga aaagtatcaa gigtitataa nattittagg
                                                                       120
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag
                                                                       180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa
                                                                       240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac
                                                                       300
attetettet gaactttaga ttttetagaa aaatatgtaa tagtgateag gaagagetet
                                                                       360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc
                                                                       420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg
                                                                       480
ancntggctt aa
                                                                       492
      <210> 198
      <211> 478
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(478)
      <223> n = A, T, C or G
      <400> 198
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa
                                                                        60
tgtntccacn acaaatcatn ttacntnagt aagaggecan ctacattgta caacatacac
                                                                       120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgeegane atancacatt
                                                                       160
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat
                                                                      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtacatan catcntgtag
                                                                      300
gagtigtggc titatgitta cigaaagica atgcagticc igiacaaaga gatggccgta
                                                                      360
agcattetag tacctetact ecatggttaa gaategtaca ettatgttta catatgtnea
                                                                       420
```

```
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa
       <210> 199
      <211> 482
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(482)
      <223> n = A,T,C or G
      <400> 199
agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
                                                                        60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
                                                                       120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                       180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                       240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga
                                                                       300
aaatttacct ggangaaaag aggetttngg etggggacca teccattgaa eetteteta
                                                                       360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg
                                                                       420
aacningach neaccettni ggaatanani etigaengen teetgaacti geteetetge
                                                                       480
ga.
                                                                       482
      <210> 200
      <211> 270
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(270)
      <223> n = A,T,C or G
      <400> 200
eggeegeaag tgeaacteea getggggeeg tgeggaegaa gattetgeea geagttggte
                                                                        60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc
                                                                       120
aaggetgage tgaegeegea gaggtegtgt caegteeeae gaeettgaeg eegtegggga
                                                                       180
cagceggaae agageeeggt gaangeggga ggeetegggg ageeeetegg gaagggegge
                                                                       240
ccgagagata cgcaggtgca ggtggccgcc
                                                                       270
      <210> 201
      <211> 419
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc feature
     <222> (1)...(419)
      <223> n = A,T,C or G
      <400> 201
ttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca
                                                                        60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                       120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca
                                                                       180
tggagtgggt gcaccetece tgtagaacet ggttacnaaa gettggggca gttcacetgg
                                                                       240
```

```
totgtgaccg toattttott gacatoaatg ttattagaag toaggatato ttttagagag
                                                                      300
tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga
                                                                      360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca
                                                                      419
      <210> 202
      <211> 509
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(509)
      \langle 223 \rangle n = A,T,C or G
      <400> 202
60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng
                                                                      120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa
                                                                      180
tacncncaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa
                                                                      240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa
                                                                      300
ggaactaaaa taaaaaaaaa cactnoogca aaggttaaag ggaacaacaa attontttta
                                                                      360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng
                                                                      420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca
                                                                      480
caatggnaat nccnccncnc tggactagt
                                                                      509.
      <210> 203
      <211> 583
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc feature
      <222> (1)...(583)
      \langle 223 \rangle n = A.T.C or G
      <400> 203
ttttttttt tttttttga cocccctctt ataaaaaaca agttaccatt ttattttact
                                                                      4640
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                      120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                      180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc
                                                                      240
attitititg totttaaaat tatotaatot ticcattitt tooctatioc aagtoaatti
                                                                      300
gettetetag ceteatttee tagetettat etaetattag taagtggett titteetaaa
                                                                      360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc
                                                                      420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg
                                                                     480
tocattttag toactaaacg atatonaaag tgocagaatg caaaaggttt gtgaacattt
                                                                     540
attcaaaagc taatataaga tatttcacat actcatctt ctg
                                                                     583
      <210> 204
     <211> 589
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ...(589)
```

```
<223> n = A,T,C or G
```

```
<400> 204
tttttttttt ttttttttt ttttttnctc ttctttttt ttganaatga ggatcgagtt
                                                                        60
tttcactctc tagatagggc atgaagaaaa ctcatcttc cagctttaaa ataacaatca
                                                                       120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc
                                                                       180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat
                                                                       240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt
                                                                       300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag
                                                                       360
cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag
                                                                       420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc
                                                                       480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat
                                                                       540
ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg
                                                                       589
      <210> 205
      <211> 545
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(545)
      <223> n = A,T,C or G
      <400> 205
tttttntttt tttttcagt aataatcaga acaatattta ttittatatt taaaattcat
agaaaagtgo ottacattta ataaaagttt gtttotoaaa gtgatoagag gaattagata
                                                                       120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat
                                                                       180
ttaagatcat agagettyta agtgaaaaga taaaatttga eetcagaaae tetgageatt
                                                                       240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat
                                                                       300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt
                                                                       420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg
                                                                       480
aaggattaga tatgtttcct ttgccaatat taaaaaaata ataatgttta ctactagtga
                                                                       540
aaccc
                                                                       545
      <210> 206
      <211> 487
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(487)
      <223> n = A,T,C or G
      <400> 206
ttttttttt tttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt
                                                                        60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna
                                                                       120
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt
                                                                      180
ecettetece accaactaat gaancageaa cattagttta attttattag tagatnatae
                                                                       240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag
                                                                      300
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt
                                                                      360
teggtgaaaa tagaetgtgt etgtetgaat caaatgatet gaeetateet eggtggeaag
                                                                      420
aactettega acegetteet caaaggenge tgecacattt gtggentetn ttgeacttgt
                                                                       480
```

ttcaaaa

```
487
      <210> 207
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) . . . (332)
      <223> n = A,T,C or G
      <400> 207
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa
                                                                         60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact
                                                                         120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana
                                                                         180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca
                                                                        240
gaaatgaagg ggccaggctt actgagcttg tocactggag ggctcatggg tgggacatgg
                                                                         300
aaaagaaggc agcctaggcc ctggggagcc ca
                                                                        332
      <210> 208
      <211> 524
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(524)
      \langle 223 \rangle n = A,T,C or G
      <400> 208
agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg
                                                                         60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat
                                                                        120
tttaaaggac atggagettg teacaatgte acaatgteac agtgtgaagg geacacteac
                                                                        180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact
                                                                        240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatocaagat atttcccaaa
                                                                        300
gtaaatagaa gtgggtcata atattaatta octgttcaca tcagcttcca tttacaagtc
                                                                        360
atgageceag acaetgaeat caaactaage ecaettagae teeteaceae cagtetgtee
                                                                        420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa
                                                                        480
aaaccattac ctgatccact teeggtaatg caccacettg gtga
                                                                        524
      <210> 209
      <211> 159
      <212> DNA
      <213> Homo sapien
      <400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg
tggccctetc ctacactetg gecagagata ccacagteaa acetggagec aaaaaggaca
                                                                        120
caaaggactc tegacecaaa etgeeccaga coeteteca
                                                                        159
      <210> 210
      <211> 256
      <212> DNA
      <213> Homo sapien
```

```
<220>
       <221> misc feature
       <222> (1)...(256)
      <223> n = A,T,C or G
       <400> 210
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc
                                                                         60
actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta
                                                                        120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat
                                                                        180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca
                                                                        240
ccaggatgct aaatca
                                                                        256
      <210> 211
      <211> 264
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(264)
      <223> n = A,T,C or G
      <400> 211 - ....
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg
                                                                         60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                        120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga
                                                                        180
ggggagatac attengaaag aggaetgaaa gaaatactea agtnggaaaa cagaaaaaga
                                                                        240
aaaaaaggag caaatgagaa gcct
                                                                        264
      <210> 212
      <211> 328
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (328)
      <223> n = A, T, C or G
      <400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa
                                                                         60
ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag
                                                                        120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag
                                                                        180
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta
                                                                        240
cccctacnac tetttactet etgganaggg ccagtggtgg tagetataag ettggccaca
                                                                        300
ttttttttc ctttattcct ttgtcaga
                                                                        328
      <210> 213
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
```

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<222> (1)...(250)
      <223> n = A,T,C or G
      <400> 213
acttatgage agagegacat atcenagtgt agaetgaata aaactgaatt etetecagtt
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                        120
cattatgcca aagganatat acatttcaat totocaaact tottoctcat tocaagagtt
                                                                        180
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct
                                                                        240
tctcatcggt
                                                                        250
      <210> 214
      <211> 444
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(444)
      <223> n = A, T, C or G
      <400> 214
acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag
                                                                         60
gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg
                                                                        120
tttatatatg cagcaacaat attcaagege gacaacaggt tattgaactt gecegecagt
                                                                        180
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac
                                                                        240
ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat
                                                                        300
ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag
                                                                        360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt
                                                                        420
actitgctct ccctaatata cctc
                                                                        444
      <210> 215
      <211> 366
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(366)
      <223> n = A,T,C or G
      <400> 215
acttatgage agagegacat atccaagtgt anactgaata aaactgaatt ctctocagtt
                                                                        60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                       120
cattatgcca aagganatat acatttcaat totccaaact tottoctcat tocaagagtt
                                                                       180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacct
                                                                       240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa
                                                                       300
tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt
                                                                       360
ggtgcc
                                                                       366
      <210> 216
      <211> 260
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc_feature
      <222> (1)...(260)
      \langle 223 \rangle n = A,T,C or G
      <400> 216
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat
                                                                        120
taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa
                                                                        180
atcaaaaatt teetnaagtt nteaagetat eatatatet ntateetgaa aaageaacat
                                                                        240
aattcttcct tccctccttt
                                                                        260
      <210> 217
      <211> 262
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(262)
      <223> n = A,T,C or G
      <400> 217
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta
tcttgcctat aattttctat tttaataagg aaatagcaaa ttggggtggg gggaatgtag
                                                                        120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt
                                                                        180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta
                                                                        240
atatccttca tgcttgtaaa gt
      <210> 218
      <211> 205
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(205)
      <223> n = A,T,C or G
      <400> 218
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca
                                                                         60
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc
                                                                        120
aggeeteece agttetactg acettigtee tranginina ngtecagggt tgetaggaaa
                                                                        180
anaaatcagc agacacaggt gtaaa
                                                                        205
      <210> 219
      <211> 114
      <212> DNA
      <213> Homo sapien
     <400> 219
tactgttttg teteagtaac aataaataca aaaagactgg ttgtgttccg gececateca
                                                                         60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga
      <210> 220
```

<211> 93

```
<212> DNA
      <213> Homo sapien
      <400> 220
actagecage acaaaaggea gggtageetg aattgettte tgetetttae atttettta
                                                                          60
aaataagcat ttagtgctca gtccctactg agt
                                                                          93
      <210> 221
      <211> 167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(167)
      \langle 223 \rangle n = A,T,C or G
      <400> 221
actangigea ggigegeaca aatatitgie gatatieeet teatetigga tieeatqaqq
                                                                         60
tettttgece ageetgtgge tetactgtag taagtttetg etgatgagga geeagnatge
                                                                        120
ccccactac cttccctgac gctccccana aatcacccaa cctctgt
                                                                        167
      <210> 222
      <211> 351
      <212> DNA
      <213> Homo sapien
     <400> 222
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc
                                                                         60
gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa
                                                                        120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa
                                                                        180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt
                                                                        240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt
                                                                        300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t
                                                                        351
      <210> 223
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      \langle 223 \rangle n = A,T,C or G
      <400> 223
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat
                                                                         60
tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga
                                                                        120
ttaaaatgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc
                                                                        180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc
                                                                        240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttggtggg ggaaanagtt
                                                                        300
ataggaccac agtetteact tetgatactt graaattaat ettetattge acttgttttg
                                                                        360
accattaagc tatatgttta aaa
                                                                        383
```

<210> 224

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<211> 320
       <212> DNA
       <213> Homo sapien
       <400> 224
 cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga
                                                                       60
 aaaagtttgt gacattgtag tagggagtgt gtacccctta ctccccatca aaaaaaaaat
                                                                      120
 ggatacatgg ttaaaggata raagggcaat attttatcat atgttctaaa agagaaggaa
                                                                      180
 gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac
                                                                      240
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcagt
                                                                      300
 tttaractcm gcattgtgac
                                                                      320
       <210> 225
       <211> 1214
       <212> DNA
       <213> Homo sapien
       <400> 225
 gaggactgca gcccgcactc gcagccctgg caggcggcac tggtcatgga aaacgaattg
                                                                       60
 ttctgctcgg gcgtcctggt gcatccgcag tgggtgctgt cagccgcaca ctgtttccag
                                                                      120
 aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc
                                                                      180
cagatggtgg aggccagcct ctccgtacgg cacccagagt acaacagacc cttgctcgct
                                                                      240
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc
                                                                      300
 atcagcattg cttcgcagtg ccctaccgcg gggaactctt gcctcgtttc tggctggggt
                                                                      360
 ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct
                                                                      420
 gaggaggtet geagtaaget etatgaceeg etgtaceace ceageatgtt etgegeegge
                                                                      480
 ggagggcaag accagaagga ctcctgcaac ggtgactctg gggggcccct gatctgcaac
                                                                      540
 gggtacttgc agggccttgt gtctttcgga aaagccccgt gtggccaagt tggcgtgcca
                                                                     600
 ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt
                                                                      660
 taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaaggaatt
                                                                      720
 caggaatate tgtteccage cectectee teaggeccag gagtecagge ceccagece
                                                                     780
 tectecetea aaccaagggt acagateece ageceeteet eceteagace caggagteea
                                                                      840
gacccccag ccctcctcc ctcagaccca ggagtccagc ccctcctccc tcagacccag
                                                                      900
 gagtecagae eccecagece etectecete agacecaggg gtecaggece ecaacecete
                                                                     960
 ctccctcaga ctcagaggtc caagccccca acccctcctt ccccagaccc agaggtccag
                                                                    1020
 gtcccagccc ctcctccctc agacccagcg gtccaatgcc acctagactc tccctgtaca
                                                                     1080
 cagtgccccc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc
                                                                     1140
 1200
 aaaaaaaaa aaaa
                                                                    1214
       <210> 226
       <211> 119
       <212> DNA
       <213> Homo sapien
       <400> 226
 acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa
                                                                      60
 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt
                                                                     119
       <210> 227
       <211> 818
       <212> DNA
       <213> Homo sapien
       <400> 227
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acaattcata gggacgacca atgaggacag ggaatgaacc oggototocc ccagcottga
                                                                        60
tttttgctac atatggggtc ccttttcatt ctttgcaaaa acactgggtt ttctgagaac
                                                                       120
acggacggtt cttagcacaa tttgtgaaat ctgtgtaraa ccgggctttg caggggagat
                                                                       180
aattttcctc ctctggagga aaggtggtga ttgacaggca gggagacagt gacaaggcta
                                                                       240
gagaaagcca cgctcggcct tctctgaacc aggatggaac ggcagacccc tgaaaacgaa
                                                                       300
gettgteece ttecaateag ecaettetga gaaceeceat etaactteet actggaaaag
                                                                       360
agggcctcct caggagcagt ccaagagttt*tcaaagataa cgtgacaact accatctaga
                                                                       420
ggaaagggtg cacceteage agagaageeg agagettaac tetggtegtt tecagagaca
                                                                       480
acctgctggc tgtcttggga tgcgcccagc ctttgagagg ccactacccc atgaacttct
                                                                       540
gccatccact ggacatgaag ctgaggacac tgggcttcaa cactgagttg tcatgagagg
                                                                       600
gacaggetet geeeteaage eggetgaggg cageaaceae tetecteece tttetcaege
                                                                       660
aaagccattc ccacaaatcc agaccatacc atgaagcaac gagacccaaa cagtttggct
                                                                       720
caagaggata tgaggactgt ctcagcctgg ctttgggctg acaccatgca cacacacaag
                                                                       780
gtccacttct aggttttcag cctagatggg agtcgtgt
                                                                       818
      <210> 228
      <211> 744
      <212> DNA
      <213> Homo sapien
      <400> 228
actggagaca ctgttgaact tgatcaagac ccagaccacc ccaggtctcc ttcgtgggat
                                                                        60
gtcatgacgt ttgacatacc tttggaacga gcctcctcct tggaagatgg aagaccgtgt
                                                                       120
tegtggeega eetggeetet eetggeetgt ttettaagat geggagteac attteaatgg
                                                                       180
taggaaaagt ggcttcgtaa aatagaagag cagtcactgt ggaactacca aatggcgaga
                                                                       240
tgctcggtgc acattggggt gctttgggat aaaagattta tgagccaact attctctggc
                                                                       300
accagattct aggccagttt gttccactga agcttttccc acagcagtcc acctctgcag
                                                                       360
gctggcagct gaatggcttg ccggtggctc tgtggcaaga tcacactgag atcgatgggt
                                                                       420
gagaaggeta ggatgettgt ctagtgttet tagetgteac gttggeteet tecaggttgg
                                                                       480
ccagacggtg ttggccactc ccttctaaaa cacaggcgcc ctcctggtga cagtgacecg
                                                                       540
ccgtggtatg ccttggcoca ttccagcagt cccagttatg catttcaagt ttggggtttg
                                                                       600
ttcttttcgt taatgttcct ctgtgttgtc agetgtcttc atttcctggg ctaagcagca
                                                                       660
ttgggagatg tggaccagag atccactcct taagaaccag tggcgaaaga cacttcttt
                                                                       720
cttcactctg aagtagctgg tggt
      <210> 229
      <211> 300
      <212> DNA
      <213> Homo sapien
      <400> 229
cgagtctggg ttttgtctat aaagtttgat ccctoctttt ctcatccaaa tcatgtgaac
                                                                        60
cattacacat cgaaataaaa gaaaggtggc agacttgccc aacgccaggc tgacatgtgc
                                                                       120
tgcagggttg ttgtttttta attattattg ttagaaacgt cacccacagt ccctgttaat
                                                                       180
ttgtatgtga cagocaacto tgagaaggto ctatttttoc acctgcagag gatocagtot
                                                                       240
cactaggete etecttgeee teacactgga gteteegeea gtgtgggtge ceactgacat
                                                                       300
      <210> 230
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 230
cagcagaaca aatacaaata tgaagagtgc aaagatctca taaaatctat gctgaggaat
                                                                       .60
gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg
                                                                       120
```

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caatataaag teetggttea caeteaggaa egagagetga eecagttaag ggagaagttg
                                                                       180
cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg
                                                                       240
gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac
                                                                       300
                                                                        301
      <210> 231
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 231
gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcattttagc
                                                                        60
caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat
                                                                       120
ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg
                                                                       180
tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt
                                                                       240
tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc
                                                                       300
                                                                       301
      <210> 232
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 232
agtaggtatt tegtgagaag tteaacaeea aaaetggaae atagttetee tteaagtgtt
                                                                        60
ggcgacagcg gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat
                                                                       120
agaagagtee atetgetgtg aaggagagae agagaaetet gggtteegte gteetgteea
                                                                       180
cgtgctgtac caagtgctgg tgccagcctg ttacctgttc tcactgaaaa tctggctaat
                                                                       240
gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact
                                                                       300
                                                                       301
      <210> 233
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 233
atgactgact teccagtaag getetetaag gggtaagtag gaggatecae aggatttgag
                                                                        60
atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg
                                                                       120
cctagaagtt acagagcatc tagctggtgc gctggcaccc ctggcctcac acagactccc
                                                                       180
gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg
                                                                       240
tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa
                                                                       300
                                                                       301
      <210> 234
      <211> 301.
      <212> DNA
      <213> Homo sapien
      <400> 234
aggteetaca categagaet catecatgat tgatatgaat ttaaaaaatta caagcaaaga
                                                                        60
cattttattc atcatgatgc tttcttttgt ttcttcttt cgttttcttc tttttcttt
                                                                       120
tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct
                                                                       180
egecteatga cageaagtte aatgtttttg ceacetgaet gaaceaette caggagtgee
                                                                       240
ttgatcacca gcttaatggt cagatcatct gcttcaatgg cttcgtcagt atagttcttc
                                                                       300
```

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t
                                                                        301
       <210> 235
       <211> 283
       <212> DNA
       <213> Homo sapien
       <400> 235
tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg
                                                                         60
aatteeetea tettttaggg aateatttae eaggtttgga gaggatteag acageteagg
                                                                        120
tgctttcact aatgtctctg aacttctgtc octctttgtt catggatagt ocaataaata
                                                                        180
atgttatett tgaactgatg etcataggag agaatataag aactetgagt gatateaaca
                                                                        240
ttagggattc aaagaaatat tagatttaag ctcacactgg tca
                                                                        283
      <210> 236
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 236
aggteeteea ceaactgeet gaageaeggt taaaattggg aagaagtata gtgeageata
                                                                        60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg
                                                                       120
tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggtatatag
                                                                       180
tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta
                                                                       240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc
                                                                       300
                                                                       301
      <210> 237
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 237
cagtggtagt ggtggtggac gtggcgttgg tcgtggtgcc ttttttggtg cccgtcacaa
                                                                        60
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg
                                                                       120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct
                                                                       180
ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta
                                                                       240
gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctccttatc
                                                                       300
                                                                       301
      <210> 238
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 238
gggcaggttt ttttttttt ttttttgatg gtgcagaccc ttgcttatt tgtctgactt
                                                                        60
gttcacagtt cagceecetg etcagaaaac caacgggcca getaaggaga ggaggaggca
                                                                       120
ccttgagact teeggagteg aggeteteca gggtteecea geccateaat cattttetge
                                                                       180
accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggattca
                                                                       240
gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta
                                                                       300
                                                                       301
      <210> 239
      <211> 239
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<212> DNA
        <213> Homo sapien
        <400> 239
  ataagcagct agggaattet ttatttagta atgteetaae ataaaagtte acataaetge
  ttctgtcaaa ccatgatact gagctttgtg acaacccaga aataactaag agaaggcaaa
                                                                          60
 cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac
                                                                         120
 attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga
                                                                         180
                                                                         239
        <210> 240
        <211> 300
        <212> DNA
        <213> Homo sapien
        <400> 240
 ggtcctaatg aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt
 gggatctgcc ctccagtgga accttttaag gaagaagtgg gcccaagcta agttccacat
                                                                          60
 gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg
                                                                         120
 ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac
                                                                        180
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc
                                                                        240
                                                                        300
       <210> 241
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 241
 gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga
 cctctttgga ggaaactcca gcagctatgt tggtgtctct gagggaatgc aacaaggctg
                                                                         60
 ctcctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag
                                                                        120
 tgtgaagaac cagcctgagg tgacagaac ggaagcaaac aggaacagcc agtctttct
                                                                        180
tectectect gteataeggt eteteteaag cateetttgt tgteagggge etaaaaggga
                                                                        240
                                                                        300
                                                                        301
       <210> 242
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 242
cegaggteet gggatgeaac caateactet gtttcaegtg acttttatea ecatacaatt
tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat
                                                                        60
gtcttcaaga atatatcatt cctttttcac tagaacccat tcaaaatata agtcaagaat
                                                                       120
cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta
                                                                       180
taagtaccca aagttttata aatcaaaagc cctaatgata accattttta gaattcaatc
                                                                       240
                                                                       300
                                                                       301
      <210> 243
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 243
aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat
ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg
                                                                        60
```

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tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt
                                                                         180
 gctggtttgt ccagatggca agacagtaga agcagaggct gcccacggga ctgtaacccg
                                                                         240.
 tractacege atgiteraga aaggaragga gacgterace aatcocattg citeratite
                                                                         300
                                                                         3.01
       <210> 244
       <211> 300
       <212> DNA
       <213> Homo sapien
       <400> 244
 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa
                                                                          60
 gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc
                                                                         120
 ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa
                                                                         180
 aggigtigta atggigaaaa cgicticcii ciilatigcc cciictiati taigigaaca
                                                                         240
 actitttigtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatc
                                                                         300
       <210> 245
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 245
gtctgagtat ttaaaatgtt attgaaatta tccccaacca atgttagaaa agaaagaggt
                                                                         60
tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt
                                                                         120
aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat
                                                                         180
gttttcaaag agcagagatg caattaaata ttgtttagca tcaaaaaggc cactcaatac
                                                                        240
agctaataaa atgaaagacc taatttotaa agcaattott tataatttac aaagttttaa
                                                                        300
                                                                        301
       <210> 246
       <211> 301
       <212> DNA
      <213> Homo sapien
      <400> 246
ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata
                                                                         60
acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata
                                                                        1.20
agtgettett gtgaaaatta aataaaacag ttaatteaaa geettgatat atgetaecae
                                                                        180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc
                                                                        240
caaatgtgtc ttacaaaaca cgttectaac aaggtatget ttacaetaec aatgeagaaa
                                                                        300
                                                                        301
      <210> 247
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 247
aggicettig geagggetea iggateagag eleaaacigg agggaaagge attiegggia
                                                                        -6∙0
gcctaagagg gcgactggcg gcagcacaac caaggaaggc aaggttgttt cccccacgct
                                                                       1:20
gtgteetgtg tteaggtgeg acacacaate eteatgggaa eaggateace eatgegetge
                                                                       180
cettgatgat caaggttggg gettaagtgg attaagggag geaagttetg ggtteettge
                                                                       240
cttttcaaac catgaagtca ggototgtat coctootttt cotaactgat attotaacta
                                                                       300
                                                                       301
```

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<210> 248
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 248
aggicetigg agaigecatt teageegaag gaetetietw tieggaagia caeceteaet
                                                                        60
attaggaaga ttcttagggg taattttct gaggaaggag aactagccaa cttaagaatt
                                                                        120
acaggaagaa agtggtttgg aagacagcca aagaaataaa agcagattaa attgtatcag
                                                                       180
gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag
                                                                       240
ctaatgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc
                                                                       300
                                                                       301
      <210> 249
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 249
gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag
                                                                        60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc
                                                                       120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc
                                                                       180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag
                                                                       240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt
                                                                       301
      <210> 250
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 250
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc
                                                                        60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc
                                                                       120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac
                                                                       180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta
                                                                       240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc
                                                                       300
                                                                       301
      <210> 251
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 251
geogaggice tacattigge coagittoec cotgeatect etccagggee cotgeeteat
                                                                        60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat
                                                                       120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct
                                                                       180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccggaa
                                                                       240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct
                                                                       300
                                                                       301
      <210> 252
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<211> 301

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<212> DNA
       <213> Homo sapien
       <400> 252
 gcaaccaatc actotytttc acytyacttt tatcaccata caatttytyy catttectca
                                                                          60
 ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata
                                                                         120
 tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa
                                                                         180
 atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt
                                                                        240
 tttataaatc aaaagcocta atgataacca tttttagaat tcaatcatca ctgtagaatc
                                                                        300
                                                                        301
       <210> 253
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 253
ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc
                                                                         60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct
                                                                        120
tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg
                                                                        180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt
                                                                        240
tccatagtgc ccacagggta ttcctcacat tttctccata ggaaaatgct ttttcccaag
                                                                        300
                                                                        301
       <210> 254
       <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 254
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg
                                                                        60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc
                                                                       120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa
                                                                       180
gaaaaaata aagetttgga etttteaagg ttgettaaca ggtaetgaaa gaetggeete
                                                                       240
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc
                                                                       300
                                                                       301
      <210> 255
      <211> 302
      <212> DNA
      <213> Homo sapien
      <400> 255
agettttttt tetetett tetetettt tecateaaaa aatagegete tetattataa
                                                                        60
attactgaaa tgtttcttt ctgaatataa atataaatat gtgcaaagtt tgacttggat
                                                                       120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggectg agtagggggg
                                                                       180
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta
                                                                      240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac
                                                                       300
aa
                                                                       302
      <210> 256
      <211> 301
      <212> DNA
     <213> Homo sapien
```

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<220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 256
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct
                                                                        60
aggaccetee tecceacace teaatecace asaccateca taatgeacee agataggeee
                                                                        120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat
                                                                        180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt
                                                                        240
gtggcctctc ggcctggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt
                                                                        300
                                                                        301
      <210> 257
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 257
gttgtggagg aactctggct tgctcattaa gtcctactga ttttcactat cccctgaatt
                                                                        60
tececaetta tttttgtett teaetatege aggeettaga agaggtetae etgeeteeag
                                                                        120
tettacetag tecagtetae eccetggagt tagaatggee atcetgaagt gaaaagtaat
                                                                        180
gtcacattac tcccttcagt gatttcttgt agaagtgcca atccctgaat gccaccaaga
                                                                       240
tettaatett cacatettta atettatete tttgaeteet etttacaceg gagaaggete
                                                                       300
                                                                       301
      <210> 258
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 258
cagcagtagt agatgeegta tgecageacg eccageacte ecaggateag caccageace
                                                                        60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc
                                                                       120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg
                                                                       180
atgicteggg cattgagget gicaataana egetgateee etgetgtatg giggigteat
                                                                       240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac
                                                                       300
                                                                       301
      <210> 259
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 259
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tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg
                                                                          60
 gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa
                                                                         120
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt
                                                                         180
 tecageteae ateteatetg catgeageae ggaeeggatg egeceaetgg gtettggett
                                                                        240
 ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg
                                                                        300
                                                                        301
       <210> 260
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 260
tttttttttt ccctaaggaa aaagaaggaa caagtctcat aaaaccaaat aagcaatggt
                                                                         60
aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa
                                                                        120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac
                                                                        180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc
                                                                        240
actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca
                                                                        300
                                                                        301
      <210> 261
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 261
aaatattega geaaateetg taaetaatgt gteteeataa aaggetttga acteagtgaa
                                                                        60
tetgetteca tecaegatte tageaatgae eteteggaea teaaagetee tettaaggtt
                                                                        120
agcaccaact attocataca attoatcago aggaaataaa ggotottoag aaggttoaat
                                                                        180
ggtgacatec aatttettet gataatttag attecteaca acettectag ttaagtgaag
                                                                        240
ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc
                                                                        300
                                                                        301
      <210> 262
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 262
gaggagagee tgttacagea tttgtaagea cagaatacte caggagtatt tgtaattgte
                                                                        60
tgtgagette ttgeegeaag teteteagaa atttaaaaag atgcaaatee etgagteace
                                                                       120
cctagacttc ctaaaccaga tectetgggg ctggaacctg gcactetgca tttgtaatga
                                                                       180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgccc
                                                                       240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat
                                                                       300
C
                                                                       301
      <210> 263
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
```

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<400> 263
 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg
 aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg
                                                                         60
 ttcttagtat tatttatggt aaataggete ttaccaettg caaataaetg gecacateat
                                                                         120
 taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg
                                                                         180
 agatgetaag geceeagaga tegtttgate caaceetett atttteagag gggaaaatgg
                                                                         240
                                                                         300
                                                                         301
       <210> 264
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 264
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc
 aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag
                                                                         60
 gtggatagat ctagaattgt aacattttaa gaaaaccata scatttgaca gatgagaaag
                                                                        120
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac
                                                                        180
                                                                        240
 accetteata taaatteaet atettggett gaggeaetee ataaaatgta teaegtgeat
                                                                        300
                                                                        301
       <210> 265
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 265
tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt
                                                                         60
cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta
                                                                        120
catattettg gaagteteta atcaactttt gttecatttg ttteatttet teaggaggga
                                                                        180
ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag
                                                                        240
cagtecaagg etttgacatg teaacaacca geataactag agtateette agagataegg
                                                                        300
                                                                        301
      <210> 266
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 266
taccgtctgc ccttcctccc atccaggcca tctgcgaatc tacatgggtc ctcctattcg
                                                                        60
acaccagate actetteet etacceacag gettgetatg ageaagagae acaaceteet
                                                                       120
ctcttctgtg ttccagcttc ttttcctgtt cttcccaccc cttaagttct attcctgggg
                                                                       180
atagagacac caatacecat aacetetete etaageetee ttataaceca gggtgcacag
                                                                       240
cacagactee tgacaactgg taaggecaat gaactgggag etcacagetg getgtgeetg
                                                                       300
                                                                       301
      <210> 267
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 267
aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg
```

```
gtteteagtg etgagteeat eeaggaaaag eteacetaga eettetgagg etgaatette
                                                                         120
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatggtct ggagtaaagc
                                                                         180
ctcattctga ttcctctct tcttttcttt caagttggct ttcctcacat occtctgttc
                                                                        240
 aattogotto agottototo otttagooot catttocaga agottottot otttggcato
                                                                        300
                                                                         301
       <210> 268
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 268
aatgteteae teaactaett eeeageetae egtggeetaa ttetgggagt tttettetta
                                                                         60
gatettggga gagetggtte ttetaaggag aaggaggaag gacagatgta actttggate
                                                                        120
tcgaagagga agtctaatgg aagtaattag tcaacggtcc ttgtttagac tcttqqaata
                                                                        180
tgctgggtgg ctcagtgagc cettttggag aaagcaagta ttattettaa ggagtaacca
                                                                        240
cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact
                                                                        300
                                                                        301
      <210> 269
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 269
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat
                                                                         60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact
                                                                        120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta
                                                                        180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca ccccaatta
                                                                        240
tacagtagea caaccacett atgtagtttt tacatgatag etetgtagaa gtttcacate
                                                                        300
t
                                                                        301
      <210> 270
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgctt ataaaattaa ttaagcctta
                                                                         60
cacaagaata catattoott ttatttotaa ggagttaaac atagatgtag ctgatgtgga
                                                                        120
gagettgetg gtgcagtgca tattggataa cactatteat ggccgaattg atcaagtcaa
                                                                        180
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa
                                                                        240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac
                                                                        300
                                                                        301
      <210> 271
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (301)
      <223> n = A,T,C or G
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<400> 271
 aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt
                                                                         60
 tttatagete atetttaggg ttgatattea gtteatgett ecettgetgt tettgateea
 gaattgcaat cacttcatca gootgtatto gotocaatto totataaagt gggtocaagg
                                                                        120
                                                                        180
 tgaaccacag agccacagca cacctettte cettggtgae tgeetteace ceatganggt
                                                                        240
 teteteetee agatganaac tgateatgeg eccacatttt gggttttata gaageagtea
                                                                        300
                                                                        301
       <210> 272
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc
                                                                         60
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga
                                                                        120
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcatccaca
                                                                        180
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc
                                                                        240
 ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag
                                                                        300
                                                                        301
       <210> 273
       <211> 301
       <212> DNA
       <213> Homo sapien
      · <220>
       <221> misc_feature
       <222> (1) ... (301)
       <223> n = A,T,C or G
       <400> 273
acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt attttttgg
                                                                        60
agagangetg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa
                                                                       120
gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc
                                                                        180
ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt
                                                                       240
gggacttnty tttacngagm accetgeeg sgegeeteg makengantt cegesanane
                                                                       300
                                                                       301
      <210> 274
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
    <400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg
                                                                        60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa
                                                                       120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca
                                                                       180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc
                                                                       240
aattgtgctt cttttgataa gaagetttet tggteatate aggaaattee aganaaagte
                                                                       300
```

```
C
                                                                         301
       <210> 275
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 275
tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg
                                                                          60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc
                                                                         120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag
                                                                         180
tcaagagact cocaggoete agegtacetg cocgggegge egetegaage egaattetge
                                                                         240
agatatecat cacactggeg gnegetegan catgeateta gaaggneeaa ttegeeetät
                                                                         300
                                                                         301
      <210> 276
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 276
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat
                                                                         60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat
                                                                        120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc
                                                                        180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagocagatc aaatttgtgt
                                                                        240
aaaactatte agtatgttte eettgettea tgtetgagaa ggeteteett caatggggat
                                                                        300
                                                                        301
      <210> 277
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(301)
      \langle 223 \rangle n = A,T,C or G
      <400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacotggga aattctaaag
                                                                         60
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg
                                                                        120
gaatcatggc actootgata ottocccasa toaacactot caatgoocca cootegtoot
                                                                        180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga
                                                                        240
gttcnctgtc gattacatct gaecagtctc ctttttccga agtecntccg ttcaatcttg
                                                                        300
                                                                        301
      <210> 278
      <211> 301
     <212> DNA
```

```
<220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
      <400> 278
taccactaca ctccagectg ggcaacagag caagacetgt etcaaagcat aaaatggaat
                                                                        60
aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca
                                                                       120
cagtetetae tgttattatg cattacetgg gaatttatat aageeettaa taataatgee
                                                                       180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaggttt
                                                                       240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt
                                                                       300
                                                                       301
      <210> 279
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 279
aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact
                                                                        60
gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc
                                                                       120
ttagaccttt accttccagc caccccacag tgcttgatat ttcagagtca gtcattggtt
                                                                       180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac
                                                                       240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag
                                                                       300
                                                                       301
      <210> 280
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 280
ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg
                                                                        60
tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct
                                                                       120
tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg
                                                                       180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga
                                                                       240
cagactatta actocacagt taattaagga ggtatgttoc atgtttattt gttaaagcag
                                                                       300
                                                                       301
      <210> 281
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 281
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc
                                                                        60
geogageaat ccaaateetg aatgaagggg catettetga aaaaggagat etgaatetea
                                                                       120
atgtggtage aatggettta tegggttata eggatgagaa gaacteeett tggagagaaa
                                                                       180
tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc
                                                                       240
```

```
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc
                                                                        300
                                                                        301
      <210> 282
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 282
caggiactac agaattaaaa tacigacaag caagiagiit ciiggcgigc acgaatigca
                                                                         60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga
                                                                        120
agogoagaag caaagoocag goagaacoat gotaacotta cagotoagoo tgoacagaag
                                                                        180
cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg
                                                                        240
cagaagcaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag
                                                                        300
                                                                        301
      <210> 283
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 283
atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag
                                                                        .60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca
                                                                        120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc
                                                                        180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttta
                                                                        240
ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt
                                                                        300
                                                                        301
      <210> 284
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 284
caggiacaaa acgciattaa giggcitaga attigaacai tigiggicti tattiactii
                                                                        60
gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa
                                                                        120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat
                                                                        180
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt
                                                                       240.
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt
                                                                       300
                                                                       301
      <210> 285
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C or G
      <400> 285
acateaceat gateggatee eccaeceatt atacgttgta tgtttacata aatactette
                                                                        60
aatgateatt agtgttttaa aaaaaataet gaaaaeteet tetgeateee aatetetaae
                                                                       120
```

```
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg
                                                                        180
 attaaatatg tetgaettet tttgaggtea caegaetagg caaatgetat ttaegatetg
                                                                        240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag
                                                                        300
                                                                        301
       <210> 286
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 286
taccactgca ticcageetg ggtgacagag tgagaeteeg tetecaaaaa aaaetttget
                                                                         60
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagattttt
                                                                        120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccaccca
                                                                        180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt
                                                                        240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg
                                                                        300
                                                                        301
      <210> 287
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 287
tacagatetg ggaactaaat attaaaaatg agtgtggetg gatatatgga gaatgttggg
                                                                         60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg
                                                                        120.
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accetetgec
                                                                        180
ccgtggttat ctcctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt
                                                                        240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc
                                                                        300
                                                                        301.
      <210> 288
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag
                                                                        60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa
                                                                       120
gatetttaaa gacaatttea agagaatatt teettaaagt tggcaatttg gagateatae
                                                                       180
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag
                                                                       240
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa
                                                                       300
                                                                       301
      <210> 289
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (301)
      <223> n = A,T,C or G
      <400> 289
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```
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgctcc tggaaactta
                                                                         60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg
                                                                        120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa
                                                                        180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga
                                                                        240
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagngga
                                                                        300
                                                                        301
      <210> 290
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C or G
      <400> 290
acactgaget ettettgata aatatacaga atgettggca tatacaagat tetatactae
                                                                        60
tgactgatct gttcatttct ctcacagetc ttacccccaa aagettttcc accctaagtg
                                                                        120
ttetgaeete ettttetaat cacagtaggg atagaggeag anecacetae aatgaacatg
                                                                        180
gagttetate aagaggeaga aacageacag aateceagtt ttaceatteg etageagtge
                                                                        240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag
                                                                        300
                                                                        301
      <210> 291
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 291
caggtaccaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac
                                                                        60
tatateaget agattttttt tetatgettt acctgetatg gaaaatttga cacattetge
                                                                       120
tttactcttt tgtttatagg tgaatcacaa aatgtattt tatgtattct gtagttcaat
                                                                       180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa
                                                                       240
acatgagett caetteeeca etaactaatt ageatetgtt atttettaac egtaatgeet
                                                                       300
                                                                       301
      <210> 292
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 292
accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tocatatagc
                                                                        60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttggtattc
                                                                       120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg
                                                                       180
ggaaatatag tasttyatga atgttnatta aattecagtt ataatagtgg ctacacacte
                                                                       240
tractaraca racagarero acagtertat atgeracaaa caratterca taartegaaa
                                                                       300
                                                                       301
```

```
<210> 293
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 293
ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc
                                                                         60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt
                                                                        120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt
                                                                        180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg
                                                                        240
ccgcgaccac gctaagecga attetgcaga tatecateac actggcggcc gctcgagcat
                                                                        301
       <210> 294
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 294
tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag
                                                                       120
tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag
                                                                       180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc
                                                                       240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt
                                                                       300
                                                                       3.01
      <210> 295
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 295
gtactette tetecectee tetgaattta attettteaa ettgeaattt geaaggatta
                                                                        60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaa gtgtctttgt ttaaaattac
                                                                       120-
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                       180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                       240
teteagaace attteaceea gacageetgt ttetateetg tttaataaat tagtttgggt
                                                                       300
tctct
                                                                       305
      <210> 296
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 296
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct
                                                                        60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttecttg
                                                                       120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac
                                                                       180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt
                                                                       240
```

```
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg
                                                                         300
                                                                         301
       <210> 297
       <211> 300
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(300)
       <223> n = A,T,C or G
       <400> 297
actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta
                                                                         60
aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtotagaga
                                                                        120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt
                                                                        180
tccatcattg ggagtgcact ggccatcct caaaatttgt ctgggctggc ctgagtggtc
                                                                        240
accgcacete ggeogegace acgctaagee gaattetgca gatatecate acaetggegg
                                                                        300
      <210> 298
      <211> 301
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
      <400> 298
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg
                                                                        60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg
                                                                       120
tgaagetete agateaatea egggaaggge etggeggtgg tggecaeetg gaaccaeeet
                                                                       180
gtcctgtctg trtacatttc actaycaggr trtctctggg cattachatt tgttccccta
                                                                       240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg
                                                                       300
                                                                       301
      <210> 299
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 299
gttttgagac ggagtttcac tettgttgee cagactggac tgcaatggea gggtetotge
                                                                        60
teactgeace etetgeetee eaggttegag eaatteteet geeteageet eccaggtage
                                                                       120
tgggattgca ggctcacgcc accataccca gctaatttt tegtatttt agtagagacg
                                                                       180.
gagtitegee atgitiggeea getggtetea aacteetgae etcaagegae etgeetgeet
                                                                       240
cggcctccca aagtgctgga attataggca tgagtcaaca cgcccagcct aaagatattt
                                                                       300
                                                                       301
      <210> 300
      <211> 301
      <212> DNA
      <213> Homo sapien
```

```
<400> 300
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga
                                                                         60
 tatgteccae acceactggg aaaggetece acctggetae tteetetate agetgggtea
                                                                        120
 gctgcattcc acaaggttct cagcctaatg agtttcacta cctgccagtc tcaaaactta
                                                                        180
 gtaaagcaag accatgacat teeceeacgg aaatcagagt ttgeeceace gtettgttae
                                                                        240
tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat
                                                                        300
                                                                        301
       <210> 301
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 301
ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc
                                                                         60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt
                                                                        120
gggaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaaagacc
                                                                        180
ctcagagctg agacacccac aacagtggga gctcacaaag accctcagag ctgagacacc
                                                                        240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt
                                                                        300
                                                                        301
      <210> 302
       <211> 301
       <212> DNA
      <213> Homo sapien
      <400> 302
aggtacacat ttagcttgtg gtaaatgact cacaaaactg attttaaaat caagttaatg
                                                                        60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac
                                                                       120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg
                                                                       180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca
                                                                       240
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg
                                                                       300
                                                                       301
      <210> 303
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 303
aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt
                                                                        60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac
                                                                       120
tggctaatgg aactaceget tgcatgttaa aaatggtggt ttgtgaaatg atcataggee
                                                                       180
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc
                                                                       240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac
                                                                       300
                                                                       301
      <210> 304
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 304
acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaat
                                                                        60
```

```
tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc
                                                                        120
 ctttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt
                                                                         180
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga
                                                                        240
 ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct
                                                                        300
                                                                        301
       <210> 305
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A, T, C or G
       <400> 305
gangtacage gtggtcaagg taacaagaag aaaaaaatgt gagtggcate ctgggatgag
                                                                         60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg
                                                                        120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag
                                                                        180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa
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ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag
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      <211> 8
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      <400> 306
Val Leu Gly Trp Val Ala Glu Leu
      <210> 307
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      <400> 307
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ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac
                                                                       150
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt
                                                                       180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca
                                                                       240
cacatagcac eggagatatg agateaacag tttettagec atagagatte acageecaga
                                                                       300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg
                                                                       360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga
                                                                       420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtgaa
                                                                       480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagoca
                                                                       540
ggtgggagec tttecccagtg ggtgtgggac atatctggca agattttgtg gcactcttgg
                                                                       600
ttacagatac tggggcagca aataaaactg aatctcg
                                                                       637
      <210> 308
      <211> 647
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                                                                         60
 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa
                                                                        120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg
                                                                        180
ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg
                                                                        240
ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt
                                                                        300
cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct
                                                                        360
cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt
                                                                        420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac
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tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca
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ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc
                                                                        600
aatgteettt ttttteteet gettetgaet tgataaaagg ggaeegt
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       <211> 460
       <212> DNA
       <213> Homo sapien
       <400> 309
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gagcacatet teagcaagag ggggaaatae teateatttt tggeeageag ttgtttgate
                                                                        180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg
                                                                       240
ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctacccag
                                                                       300
ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc
                                                                       360
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat
                                                                       420
ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt
                                                                       460
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                                                                       120
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tetgtgagaa
                                                                       180
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa
                                                                       240
taatetttat ggeagagaaa getaaaatee tttagettge gtgaatgate aettgetgaa
                                                                       300
ttcctcaagg taggcatgat gaaggaggt ttagaggaga cacagacaca atgaactgac
                                                                       360
ctagatagaa agcettagta tacteageta ggaatagtga ttetgaggge acaetgtgae
                                                                       420
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc
                                                                       480
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      <212> DNA
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 catttacago atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa
                                                                          180
 attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg
                                                                          240
 tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa
                                                                          300
 aaaatgggga aactetgaag ggttttaagt atettaeetg aagetaeaga etecataaee
                                                                          360
 tetetttaca gggageteet geageceeta cagaaatgag tggetgagat tettgattge
                                                                          420
 acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa
                                                                          480
 agttetataa actgtagtnt acttatttta atecccaaag cacagt
                                                                          526
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       <211> 500
       <212> DNA
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       <220>
       <221> misc_feature
       <222> (1)...(500)
       \langle 223 \rangle n = A, T, C \text{ or } G
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 tcatttctga aagcagttga gocactttat tccaaagtac actgcagatg ttcaaactct
                                                                          60
                                                                         120
ccattetete ttecetteca ectgecagtt ttgctgacte tcaacttgte atgagtgtaa
                                                                         180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg
                                                                         240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atcccctctt
tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct
                                                                         300
                                                                         360
tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct
                                                                         420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt
                                                                         480
tagtettaat tatetattgg
                                                                         500
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      <211> 718
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(718)
      <223> n = A,T,C or G
      <400> 313
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tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat
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ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa
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gtagtgacat gtttttgcac atttccagec cttttaaata tccacacaca caggaagcac
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aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga
                                                                        300
geetegeeet gtgeetgnte oegettgtga gggaaggaca ttagaaaatg aattgatgtg
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tteettaaag gatggeagga aaacagatee tgtegtggat atetattga acgggattae
                                                                        420
```

					•
agatttgaaa tgaagtcaca	aagtgagcat	taccaatgag	aggaaaaca	g acgagaaat	480
cergaryger cacaagacat	gcaacaaaca	l aaatggaata	1 ctotoatoa	. 200200200	540
aaccagagag gagacaccac	ggggcagagc	r tcaggattet	garcetact	T CCTARALA	
cyclacacca accaeteeta	LECECTACCCE	-caaacaacct	gtngaatat	- tasattas	600
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•				- caaanege	718
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			•	-	
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gaccccatt ctgaagatgt	ctggaacctc	taccagcago	atgatgatag	CCCCaatage	: 120
agtcaccagc teceegacca	gccggatatc	gtccttaggg	greatgrage	cttcctacgac	180
tagettetge tgtaagaggg	tgttgtcccq	gagactcata	Contractor	tectecage	240
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<211> 151					
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			* * * * * * * * * * * * * * * * * * *		
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agactgggca agactcttac	gccccacact	gcaatttoot	Cttattacca	tarccattta	60
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cattcaggga gctctggttg	caatattagt	t	-5-55-5	cgaccggacc	120 151
					121
<210> 317	•			4.	:
<211> 151	•	*		• •	
<212> DNA					
<213> Homo sapie	n				
•					. •
<400> 317		• • •	•		٦.
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atcttcattt atctctggcc	ttaacccraa	CtCctgagge	tacaacaaca	aacggctcaa	60
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3 123300		<del>-</del>		•	151
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<212> DNA		•			100

## 107

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                                                                         120
 gttcaatyaa aaagacactt ancccatgtg g
                                                                         151
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       <211> 461
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       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(461)
       \langle 223 \rangle n = A,T,C or G
       <400> 324
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agaagtggtc agctaaagga atccaggttg ttggttggac tgttaatacc tttgatgaaa
                                                                        120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact
gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccagggge
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ctcatacagg gatatcaaaa taccctttgt gctacccagg ccctggggaa tcaggtgact
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cacacaaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt
                                                                        360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga
                                                                        420
aaaaacgcac aagagcccct gccctgccct agctgangca c
                                                                        461
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       <211> 400
      <212> DNA
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                                                                        120
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt
                                                                        180
tctataaatg aatgtgctga agcaaagtgc ccatggtggc ggcgaagaag agaaagatgt
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gttttgtttt ggactetetg tggteeette caatgetgtg ggttteeaac caggggaagg
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gtcccttttg cattgccaag tgccataacc atgagcacta cgctaccatg gttctgcctc
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gaactectae accateggge tgggeetgea cagtettgag geegaeeaag ageeagggag
                                                                       180
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ccagatggtg gaggecagec teteegtacg geacecagag tacaacagae cettgetege
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taacgacete atgeteatea agttggacga atcegtgtee gagtetgaca ceatceggag
                                                                   300
catcagcatt gettegeagt gecetacege ggggaactet tgeetegttt etggetgggg
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tetgetggeg aacggeagaa tgeetacegt getgeagtge gtgaacgtgt eggtggtgte
                                                                   420
tgaggaggtc tgcagtaagc tctatgaccc gctgtaccac cccagcatgt tctgcgccgg
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cggagggcaa gaccagaagg actcctgcaa cggtgactct ggggggcccc tgatctgcaa
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                                                                   540
                                                                   600
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ttaactctgg ggactgggaa cccatgaaat tgacccccaa atacatcctg cggaaggaat
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                                                                   780
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                                                                   960
ceteceteag acteagaggt ecaageeeee aacceeteet teeccagace cagaggteea
                                                                  1020
ggtcccagcc cetectecet cagacecage ggtccaatgc cacetagact etceetgtac
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1200
aaaaaaaaa aaaaa
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<210> 327

<211> 220

<212> PRT

<213> Homo sapien

<400> 327

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  atccgcagtg ggtgctgtca gccacacact gtttccagaa ctcctacacc atcgggctgg
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  geetgeacag tettgaggee gaccaagage cagggageca gatggtggag geea
                                                                         234
        <210> 329
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        <213> Homo sapien
        <400> 329
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 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
                                  25
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
       <210> 330
       <211> 70
       <212> DNA
       <213> Homo sapien
       <400> 330
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                                                                         60
 gctgcagcca
       <210> 331
       <211> 22
       <212> PRT
       <213> Homo sapien
       <400> 331
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
Val Ser Gly Ser Cys Ser
             20
       <210> 332
       <211> 2507
       <212> DNA
       <213> Homo sapien
       <400> 332
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                                                                        60
 tgcccttcct tctgtatatg gctgcgccc aaatcaggaa aatgctgtcc agtggggtgt
```

						A •
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tcgggaagga	qacaqccaaa	a gagetagete	, edacadead	tocaggage	t ttagcttgcc	
gggatgtgg	aaaqqqqqaa	ttaataacca	. agagaggaga	cegageaca	a gggaaccagc	240
aggtgttggt	gcggaaacto	. gaectotete	. atactaect	tattacae	a gggaaccagc t tttgctaagg	300
gcttcttag	tgaggaaaac	rectorec	ttttatato	Cactegage	tttgctaagg gtgatgatgt	360
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cccaggaact	qqcccqqaqa	Ctaaaaggct	ctacageas	goragecaac	gtacaccctg	660
gcacagtcca	atctgaactg	gttcggcact	Catctttcat	gacycatect	gtacaccctg tggtggcttt	720
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                                                                       240
aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc
                                                                       300
ctgattetta acattgtett taatgaccae aagacaacca acag
                                                                       344
     <210> 342
      <211> 592
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<400> 342
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                                                                        120
cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg
                                                                        180
accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact
                                                                        240
teceteagaa gagtgtaaag aaaagteaga gatgetataa tageagetat tetaattgge
                                                                        300
aagtgccact gtggaaagag ttcctgtgtg tgctgaagtt ctgaagggca gtcaaattca
                                                                        360
teageatggg etgtttggtg caaatgeaaa ageacaggte tttttageat getggtetet
                                                                        420
occytytect tatycaaata atcytettet tetaaattte teetagyett cattttecaa
                                                                        480
agttettett ggtttgtgat gtettttetg ettteeatta attetataaa atagtatgge
                                                                        540
ttcagecaec cactettege ettagettga cegtgagtet eggetgeege tg
                                                                        592
      <210> 343
      <211> 382
      <212> DNA
      <213> Homo sapien
      <400> 343
ttettgaeet eeteeteett caageteaaa caccacetee ettatteagg aeeggeaett
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cttaatgttt gtggctttct ctccagcctc tcttaggagg ggtaatggtg gagttggcat
                                                                        120
cttgtaactc teetttetee tttetteece tttetetgee egeettteec ateetgetgt
                                                                        180
agacticitg attgicagic tytgicacat ccagigatig tittggittc tgitcccttt
                                                                       240
ctgactgccc aaggggetea gaaccecage aatecettee titeactace ttettittig
                                                                        300
ggggtagttg gaagggactg aaattgtggg gggaaggtag gaggcacatc aataaagagg
                                                                        360
aaaccaccaa gctgaaaaaa aa
                                                                       382
      <210> 344
      <211> 536
      <212> DNA
      <213> Homo sapien
      <400> 344
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caataggeca cataaaettg getggatgga aceteacaat aaggtggtea eetettgttt
                                                                       150
gtttaggggg atgccaagga taaggccagc tcagttatat gaagagaagc agaacaaaca
                                                                       180
agtettteag agaaatggat geaateagag tgggateeeg gteacateaa ggteacacte
                                                                       240
caccttcatg tgcctgaatg gttgccaggt cagaaaaatc caccccttac gagtgcggct
                                                                       300
tegacectat atecceegee egegteeett tetecataaa attettetta gtagetatta
                                                                       360
ccttcttatt atttgatcta gaaattgeec tecttttacc cctaecatga gccctacaaa
                                                                       420
caactaacct gecactaata gttatgteat ecetettatt aateateate etagecetaa
                                                                       480
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa
                                                                       536
      <210> 345
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 345
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tgaatgaage ecceatettt gtgeeteetg aaaagagagt ggaagtgtee gaggaetttg
                                                                       120
gcgtgggcca ggaaatcaca toctacactg cocaggagcc agacacattt atggaacaga
                                                                       180
aaataacata teggatttgg agagacactg ecaactgget ggagattaat eeggacactg
                                                                       240
gtgccatttc c
                                                                       251
```

```
<210> 346
        <211> 282
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(282)
        <223> n = A, T, C \text{ or } G
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 ctaagtcttg ttaccaaaaa aaggaaaaag aaaagatctt ctcagttaca aattctggga
                                                                          60
 agggagacta tacctggctc ttgccctaag tgagaggtct tccctcccgc accaaaaaat
                                                                         120
 agaaaggett tetattteac tggcccaggt agggggaagg agagtaaett tgagtetgtg
                                                                         180
                                                                         240
 ggtctcattt cccaaggtgc cttcaatgct catnaaaacc aa
                                                                         282
       <210> 347
       <211> 201
       <212> DNA
       <213> Homo sapien
       <220>
      <221> misc_feature ;
       <222> (1)...(201)
       <223> n = A,T,C or G
       <400> 347
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taaatataac ttttaaaana ntactancag cttttaccta ngctcctaaa tgcttgtaaa
                                                                         60
tetgagaetg aetggaecea eccagaecea gggeaaagat acatgttace atateatett
                                                                        180
tataaagaat tttttttgt c
                                                                        201
      <210> 348
       <211> 251
       <212> DNA
      <213> Homo sapien
      <400> 348
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agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgcccctg ggcaggcaga
                                                                        120
aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg
                                                                        180
ggggaaggtt ttattataga acteccaaca geccaectea etectgecae ecaecegatg
                                                                        240
gccctgcctc c
      <210> 349
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 349
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aaccectgag gatgccagag ctatgggtcc agaacatggt gtggtattat caacagagtt
                                                                        60
cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt
                                                                       120
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca
                                                                       180
```

```
actoctggtt t
                                                                         251
        <210> 350
        <211>-908
        <212> DNA
        <213> Homo sapien
        <400> 350
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 agecegeeeg gtgaageteg etgettteee taceteetta agtgaetgee aaaegeeeae
                                                                          60
 eggetggaat tgetetggtt atgatgacag agaaaatgat etetteetet gtgacaccaa
                                                                         120
                                                                         180
 cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca
 gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa
                                                                         240
 tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tggtgtcaga
                                                                         300
 aggatcatgt gccacagtcc atgaaggctc tggagaaact agtcaaaagg agacatccac
                                                                         360
 ctgtgatatt tgccagtttg gtgcagaatg tgacgaagat gccgaggatg tctggtgt
                                                                         420
 gtgtaatatt gactgttctc aaaccaactt caatcccctc tgcgcttctg atgggaaatc
                                                                        480
 ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt
                                                                        540
 catgiciting ggicgatgic aagataacac aactacaact actaagicig aagatgggca
                                                                        600
 ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca
                                                                        6.60
 ccacatacct tgtecggaac attacaatgg cttctgcatg catgggaagt gtgagcattc
                                                                        720
 tatcaatatg caggagecat ettgeaggtg tgatgetggt tatactggac aacactgtga
                                                                        780
                                                                        840
 aaaaaaggac tacagtgttc tatacgttgt tcccggtcct gtacgatttc agtatgtctt
                                                                        900
 aatcgcag
                                                                        908
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       <211> 472
       <212> DNA
       <213> Homo sapien
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gtcaaacctt aatgecattg ttattgtgaa ttaggattaa gtagtaattt tcaaaattca
                                                                        60
cattaacttg attttaaaat cagwittgyg agtcattiac cacaagctaa atgigtacac
                                                                        120
tatgataaaa acaaccattg tattootgtt tttotaaaca gtootaattt otaacactgt
                                                                       180
atatateett egacateaat gaactitgtt tiettitaet eeagtaataa agtaggeaca
                                                                       240
gatetyteca caacaaactt geetteteat geettyeete teaccatyet etyetecagy
                                                                       300
tragreecet tetggerigt tegetteger aaaaacetaa totgettett getteettg
                                                                       360
gtaatatata tttagggaag atgttgcttt gcccacacac gaagcaaagt aa
                                                                       420
                                                                       472 --
      <210> 352
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 352
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tgtggataag gccaggtcaa tggctgcaag catgcagaga aagaggtaca teggagegtg
                                                                        60
caggetgegt teegteetta egatgaagae taegatgeag titeeaaaca tigeeactae
                                                                       120
atacatggaa aggagggga agccaaccca gaaatgggct ttctctaatc ctgggatacc
                                                                       180
                                                                      240
aataagcaca a
                                                                       251
      <210> 353
      <211> 436
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## <213> Homo sapien

<400> 353	
ttttttttt tttttttt ttttttacaa caatgcagtc atttattat tg	
cacattatgg tattattact atactgatta tattatcat gtgacttcta at	agtatgtg 6(
gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata ga	taraaaat 120
gataaggcaa cttatacatt gacaatccaa atccaagag acagaagata ga	cattaaca 180
gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tg	ggaaatga 240
gggggacaaa tggaagccar atcaaatttg tgtaaaacta ttcagtatgt tt	cccttgct 300
tcatgtctga raaggctctc ccttcaatgg ggatgacaaa ctccaaatgc cattaacagaat actagattca cactagaaga	cacaaatg 360
ttaacagaat actagattca cactggaacg ggggtaaaga agaaattatt tta	Ctataaaa 420
333°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°	436
<210> 354	
<211> 854	
<212> DNA	•
<213> Homo sapien	
1223 nomo sapten	•
<400> 354	
CCTTTCtag ttgaccagtt ttgaccagtt	•
ccttttctag ttcaccagtt ttctgcaagg atgctggtta gggagtgtct gca	aggaggag 60
- JJ WYWWWCCU WWAAAAAAAAAA	_
and a second decadadded adalacatic accepted a	- <b>-</b>
: " " " " " " " " " " " " " " " " " " "	
a baracactatt atayyaycac ftogganana toatataaaa	
salarated agradegggg radaldeded fartafatat tastrontan	
	•
The state of the s	•
- State detection coadatated adcadeage tractactt can	ggctgtc 840
acacgggatg tcag	854
-210 255	•••
<210> 355	
<211> 676	e .
<212> DNA	
<213> Homo sapien	
.400	
<400> 355	
gaaattaagt atgagetaaa tteeetgtta aaaeetetag gggtgaeaga tete	ettcaac 60
	· .
The standard of the same and th	
- 33-44-53 CCycadaaay CCyaCCaaed agagcycant teaacacaaa	
TO STORE THE PROPERTY OF THE P	
- 3-3-0-1-10 Cacyycoadd dddctdttca cacreracac acarerana	
The state of the s	
- 33-3	
and decade and decide degree day at a ant cach the	taaggg 600
gcttaaagaa aaccag	
	676

<210> 356

<211> 574

```
<212> DNA
       <213> Homo sapien
       <400> 356
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                                                                        120
 caagetteee atttgtagat eteagtgeet atgagtatet gacacetgtt eetetetea
                                                                        180
 gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc
                                                                        240
 aaaagtccac aaaactgcag tctttgctgg gatagtaagc caagcagtgc ctggacagca
                                                                        3.00
 gagttetttt ettgggeaac agataaccag acaggactet aategtgete ttatteaaca
                                                                        360
 ttettetgte tetgeetaga etggaataaa aageeaatet etetegtgge acagggaagg
                                                                        420
 agatacaago togtttacat gtgatagato taacaaaggo atotacogaa gtotggtotg
                                                                        480
 gatagacggc acagggagct cttaggtcag cgctgctggt tggaggacat toctgagtcc
                                                                        540
 agetttgcag cetttgtgca acagtaettt ceca
                                                                        574
       <210> 357
       <211> 393
       <212> DNA
       <213> Homo sapien
       <400> 357
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                                                                         60
taatatggkg kettgtteac tataettaaa aatgeaceae teataaatat ttaatteage
                                                                        120
aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaag
                                                                        180
atagatataa ttattocagt ttttttaaaa ottaaaarat attocattgo ogaattaara
                                                                       240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa
                                                                        300
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct
                                                                       360
tttttttctt tttctgtttt tttttttt tac
                                                                       393
       <210> 358
      <211> 630
       <212> DNA
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                                                                       120
gcatagagta gggaagctaa tocagcacag ggaggtcaca gagacatccc taaggaagtg
                                                                       180
gagtttaaac tgagagaagc aagtgcttaa actgaaggat gtgttgaaga agaagggaga
                                                                       240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact
                                                                       300
gaaagagage tagaacaget ggageegtte teeggtgtaa agaggagtea aagagataag
                                                                       360
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt otacaagaaa
                                                                       420
tractgaagg gagtaatgtg acattacttt tracttragg atggerattr taactoragg
                                                                       480
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt
                                                                       540
gaaagacaaa aataagtggg gaaattcagg ggatagtgaa aatcagtagg acttaatgag
                                                                       600
caagccagag gttoctocac aacaaccagt
                                                                       630
      <210> 359
      <211> 620
      <212> DNA
      <213> Homo sapien
      <400> 359
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taattaaaaa atgctactaa tatagaaaat ttacaatcag aaaaataaat attcagggag
                                                                       120
```

```
ctcaccagaa gaataaagtg ctctgccagt tattaaagga ttactgctgg tgaattaaat
 atggcattcc ccaagggaaa tagagagatt cttctggatt atgttcaata tttatttcac
                                                                         180
 aggattaact gttttaggaa cagatataaa gcttcgccac ggaagagatg gacaaagcac
                                                                         240
                                                                         300
 aaagacaaca tgatacctta ggaagcaaca ctaccctttc aggcataaaa tttggagaaa
 tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt
                                                                         360
 aatgtaagat aactttataa gaattetggg teaaataaaa ttetttgaag aaaacateea
                                                                         420
 aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca
                                                                         480
 aacaaaaagc tcacaccaaa caaaaccatc aacttatttt gtattctata acatacgaga
                                                                         540
                                                                         600
 ctgtaaagat gtgacagtgt
                                                                         620
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       <211> 431
        <212> DNA
       <213> Homo sapien
       <400> 360
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 tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa
                                                                         60
 tactcatcat ttttggccag cagttgtttg atcaccaaac atcatgccag aatactcagc
                                                                        120
 aaaccttctt agctcttgag aagtcaaagt ccgggggaat ttattcctgg caattttaat
                                                                        180
 tggactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgtcact
                                                                        240
 agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg
                                                                        300
 tgatgccaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcggtgtgt
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                                                                        420.
 agattcttag t
                                                                        431
       <210> 361
       <211> 351
       <212> DNA
       <213> Homo sapien
       <400> 361
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actttcttct cagaagatag ggcacagcca ttgccttggc ctcacttgaa gggtctgcat
                                                                         60
ttgggtcctc tggtctcttg ccaagtttcc cagccactcg agggagaaat atcgggaggt
                                                                        120
ttgacttcct ccggggcttt cccgagggct tcaccgtgag ccctgcggcc ctcagggctg
                                                                        180
caatcctgga ttcaatgtct gaaacctcgc tctctgcctg ctggacttct gaggccgtca
                                                                       240
ctgccactct gtcctccagc tctgacagct cctcatctgt ggtcctgttg t
                                                                       300
                                                                       351
      <210> 362
      <211> 463
      <212> DNA
      <213> Homo sapien
      <400> 362
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tgtagatgag ccggctgaag atcttgcgca tgcgcggctt cagggcgaag ttcttggcgc
                                                                        60
ccccggtcac agaaatgacc aggttgggtg ttttcaggtg ccagtgctgg gtcagcagct
                                                                       120
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttccct ttcttcccca
                                                                       180
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttccttggtg tgtttcttgt
                                                                       240
agttccattt ctcactttgg ttgatctggg tgccttccat gtgctggctc tgggcatagc
                                                                       300
cacacttgca cacattetee etgataagea egatggtgtg gacaggaagg aaggatttea
                                                                       360
ttgagcctgc ttatggaaac tggtattgtt agcttaaata gac
                                                                       420
                                                                       463
      <210> 363
```

<211> 653

```
<212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(653)
       \langle 223 \rangle n = A,T,C or G
       <400> 363
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                                                                          60
 ctcttggnga ttctgggtga catcttcatg aatggcaacc gtgccagwga ggctgtcctc
                                                                         120
 tgggaggcac tacgcaagat gggactgcgt cctggggtga gacatcctct ccttggagat
                                                                         180
 ctaacgaaac ttctcaccta tgagttgtaa agcagaaata cctgnactac agacgagtgc
                                                                         240
 ccaacagcaa ccccccggaa gtatgagttc ctctrgggcc tccgttccta ocatgagasc
                                                                         300
 tagcaagatg naagtgttga gantcattgc agaggttcag aaaagagacc cntcgtgact
                                                                         360
 ggtctgcaca gttcatggag gctgcagatg aggccttgga tgctctggat gctgctgcag
                                                                         420
 ctgaggccga agcccgggct gaagcaagaa cccgcatggg aattggagat gaggctgtgt
                                                                         480
ntgggccctg gagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag
                                                                        540
attitggaga tecniggice agaatteeat tracettetg ggecagatac caecagaatg
                                                                        600
 cocgetecag atteceteag acetttgeeg greecattat tggtestggt ggt
                                                                        653
       <210> 364
       <211> 401
       <212> DNA
       <213> Homo sapien
      <400> 364
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acaaagccaa tgaatgactc taaaaacaat atttacattt aatggtttgt agacaataaa
                                                                        120
aaaacaaggt ggatagatct agaattgtaa cattttaaga aaaccatagc atttgacaga
                                                                        180
tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata
                                                                        240
cattleacae ectteatata aatteactat ettggettga ggeacteeat aaaatgtate
                                                                        300
acgtgcatag taaatcttta tatttgctat ggcgttgcac tagaggactt ggactgcaac
                                                                        360
aagtggatgc gcggaaaatg aaatcttctt caatagccca g
                                                                        401
      <210> 365
      <211> 356
      <212> DNA
      <213> Homo sapien
      <400> 365
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                                                                         60
atgittcagt gctagagcgt aggaatagac cctggcgtcc actgtgagat gttcttcagc
                                                                        120
taccagagca tcaagtetet geageaggte attettgggt aaagaaatga ettocacaaa
                                                                        180
ctctccatcc cctggctttg gcttcggcct tgcgttttcg gcatcatctc cgttaatggt
                                                                        240
gactgtcacg atgtgtatag tacagtttga caagcctggg tocatacaga ccgctggaga
                                                                        300
acatteggea atgreecett tgtagecagt ttettetteg ageteeegga gageag
                                                                        356
      <210> 366
      <211> 1851
      <212> DNA
      <213> Homo sapien
      <400> 366
tratraccat typecagrage gycaocytea greagytete etyggaater cacatgagta
```

```
cttecgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt
 tcacttcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga
                                                                        120
 ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg
                                                                        180
 canattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag
                                                                        240
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<213> Homo sapien

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	salar de la	420
	The state of the s	480
		540
		600
	services agoctagged codedicace adagaagare recessor conserve	660
	strange of the strang	720
		780
	substitution decreased galactaged Edecageria argreetes concerns	840
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	STATE OF STATE CARDINATION OF THE CONTRACT OF	
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	Transcribed aggraragat clacidatit tatelicana aractosse contracto	1020
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                                                                   1680
agaacacctg aaagccagca atttcctgac actgagaatg aagagtatca cagtgacgaa
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1800
attotgatto atgaagaaaa goagatagaa gtggttgaaa aaatgaatto tgagotttot
                                                                   1860
cttagttgta agaaagaaaa agacatcttg catgaaaata gtacgttgcg ggaagaaatt
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                                                                   2000
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<213> Homo sapien

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aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca
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tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gaaaagatct
                                                               1560
caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa
                                                               1620
gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc
                                                               1680
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                                                               1740
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<211> 329

<212> PRT

<213> Homo sapien

<400> 376

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	Leu			85					90			•		95	Val
	Ala		100					105				. 187	110	_	_
	Val	115			•		120					125		_	
	Lys 130					135					140				=
145	Asn				150					155					160
	Asn			165					170					175	Cys
	Leu		180					185			-		190		
	Gln	195					200				-	205			_
	Asp 210					215					220				_
225	Val				230					235					240
Gly	Ala	Asp	Ile	Glu 245	Ser	Lys	Asn	Lys	His 250	Gly	Leu	Thr	Pro	Leu 255	Leu
•	Gly		260	•				Gln 265	Val				270	Ile	_
Lys	Lys	Ala 275	Asn	Leu	Asn	Ala	Leu 280	Asp	Arg	Tyr		Arg	Thr	Ala	Leu
Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile			Pro	Len	T.011

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                                         315
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                            40
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
                        55.
Val Val Lys Leu Xaa Leu Asp Arg Cys Gln Leu Asp Val Leu Asp
                    70
                                        75
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
                                105
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
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His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
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Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	_	Ser
Gly	Lys	Ser	Lys		Gly	Ala	Trp			Tyr	Asp	Asp 125	Ser	Ala	Phe
Met	Glu 130	Pro	Arg	Tyr	His	Val 135	Arg	Gly	Glu	Asp	Leu 140	Asp	Lys	Leu	His
145					150					155					Met 160
				165					170					175	Ala
			180					185					190		Leu
		195					200					205		_	Thr
	210					215				Asp	220				
225					230					235					Asn 240
				245					250	Asp Ser				255	3
			260					265		Ser			270		
		275					280		•			285			•
	290					295					.300				
305					310					315					320 Leu
				325					330	Ser				335	
			340					345		Lys			350		
	Ser	355		1			360			Ser		365			
Pro	370				Val	375				٠.	380				Ser
385 Ser	Val	Lys	Lys	Pro	390 Phe	Gly	Leu	Arg		395 Lys	Met	Gly	Lys	Trp	400 Cys
Cys	Arg	Cys	Phe 420	405 Pro	Cys	Cys	Arg		410 Ser	Gly	Lys	Ser		415 Val	Gly
Thr	Ser	Gly 435		His	Asp	Asp	Ser	425 Ala	Met	Lys	Thr		430 Arg	Ser	Lys
Met	Gly 450		Trp	Суз	Arg	His 455		Phe	Pro	Суз	Cys 460	445 Arg	Gly	Ser	Gly
Lys 465	Ser	Asn	Val ·	Gly	Ala 470		Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys 480
Thr	Leu	Arg	Asn	Lys 485		Gly	Lys	Trp	Cys 490		His	Cys		Pro 495	Cys:
Cys	Arg	Gly	Ser 500		Lys	Ser	Lys	Val 505		Ala	Trp	Gly	Asp 510	Tyr .	Asp
Asp	Ser	Ala 515	Phe	Met	Glu	Pro	Arg 520	Tyr	His	Val	Arg	Gly 525	Glu	Asp	Leu

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Leu 545			Met	Leu	Arg 550	Asp		Asp	Val		Lys		Asp	Lys	Gln
	Arg	Thr	Ala		His		Ala	Ser				Asn	Ser		560 Val
Val	Lys	Leu				Arg	Arg			Leu	Asn	Val	Leu	575 Asp	
Lys	Lys				Leu	Ile				Gln	Cys	Gln	590 Glu	Asp	Glu
Сув		595 Leu		Leu	Leu				Thr	Asp	Pro	605 Asn		Pro	Asp
Glu	610 Tyr	Gly	Asn	Thr	Thr	615 Leu		Tvr	Ala	Ile	620 Tyr	Asn	GDi	Den	Lare
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				645					650					655	
			660					665					670		Lys
Gln	Gln	Val 675	Val	Lys	Phe	Leu	Ile 680	Lys	Lys	Lys	Ala	Asn 685	Leu	Asn	Ala
Leu	Asp 690	Arg	Tyr	Gly	Arg	Thr 695		Leu	Ile	Leu	Ala 700		Cys	Cys	Gly
Ser 705	Ala	Ser	Ile	Val	Ser 710	Leu	Leu	Leu	Glu	Gln 715		Ile	Asp	Val	-
-	Gln	Asp	Leu	Ser		Gln	Thr	Ala	Arg	Glu-	Tyr	Ala	Val	Ser	720 Ser
Uic	uic	uic	นาไ	725	Crra	C3 =	7		730		_			735	
ii.r.s	nis	nıs	740	116	Cys	6111	Leu	745	Ser	Asp	тух	гÀг	750	Lys	Gln
		755					760			Pro		765	Asp		- "
	770				•	775				Lys	780				
785			-		790					Ile 795		_	_	_	800
Arg	Glu	Val	Glu	Glu 805	Glu	Met	Lys	Lys	His 810	Glu	Ser	Asn	Asn	Val 815	Gly
Leu	Leu	Glu	Asn. 820	Ļeu	Thr	Asn	Gly	Val 825	Thr	Ala	Gly	Asn	Gly 830	Asp	Asn
Gly	Leu	Ile 835	Pro	Gln						Pro			Gln		
Pro	Asp 850	Asn	Glu	Ser	Glu	Glu 855	Tyr	His	Arg	Ile					
Asp	Tyr	Lys	Glu	Lys			Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	
865 Pro	Glu	Gln	Asp	Leu	870 Lys	Leu	Thr	Ser	Glu	875 Glu		Ser	Gln	Arg	880 <b>Le</b> u
				885					890					895	
			900					905		<b>Gl</b> u			910		
		915					920			Val	-	925			
Leu	Thr 930	Asn	Gly	Ala	Thr		Gly	Asn	Gly	Asp		Gly	Leu	Ile	Pro
		Lys	Ser	Arg	Thr	935 Pro	Glu	Ser	-Gln	Gln	94·0 Phe	Pro	Aso	Thr	Glu
945					950					955			_		960
ASN	GIU	GIU	ıyr	His	ser	qzA	Glu	Gln	Asn	Asp	Thr.	Gln	Lys	Gln	Phe

				965			_		970					975	
Cys	Glu	Glu	Gln 980	Asn	Thr	Gly	Ile	Leu 985		Asp	Glu	Ile	Leu 990	Ile	His
Glu	Glu	Lys 995	Gln	Ile	Glu	Val	Val	Glu		Met	Asn	Ser 100	Glu	Leu	Sei
Leu	Ser 101	Cys	Lys	Lys	Glu	Lys 101	Asp		Leu	His	Glu 102	Asn		Thr	Leu
Arg 102	Glu 5	Glu	Ile	Ala	Met 103	Leu 0	Arg	Leu	Glu	Leu 103	Asp		Met	Lys	His
Gln	Ser	Gln	Leu	Pro 104		Thr	His	Met	Val	Val		Val	Asp	Ser	Met
			106	0			Lys	106	5				1070	Lys )	Met
		1079	5				Phe 108	0				1089	Ser	Gly	
	1090	)				109					1100	0			
110	5				1110	0	Trp			1119	5				112
				1129	5		Val	•	1130	)				1139	5
			1140	)			Asn	1145	5				1150	)	
		1155	5				Ser 1160	) .				1165	5	•	
	1170	) .				1175					1180	<u>י</u>	-		
Gly 1185	Glu- i	Asp	Leu	Asp	Lys 1190	Leu )	His	Arg	Ala	Ala 1195		Trp	Gly	Lys	Val
Pro	Arg	Lys	Asp	Leu 1205	Ile	Val	Met	Leu	Arg 121(	Asp		Asp	Val.	Asn 1215	Lys
	٠.		1220	)			Ala	1225	His 5	Leu			1230	Asn	Gly
		1235	5				Leu 1240	) :				1245	Gln	Leu	
	1250	) . :				1255					1260	)			
1265	5		•		1270	)	Met.			1275	5		•	•	128
				1285	5		Asn	•	1290	)				1295	
			1300	)			Lys	1305	5				1310	١.	
		1315					Gly 1320	) .		•		1325	i	٠.	
	1330		-			1335			•		1340	)	٠.		
1345	5				1350	)	Tyr			1355	•	٠		*	136
		•		1365	•	. •	Ile		1370	)				1375	Asn
			1380	)			Leu	1385	<b>5</b>				Arg 1390	Glu	Tyr
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<211> 656

<212> PRT

<213> Homo sapien

<400> 379

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Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
35 40 45

His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
50 55

Cys 65	Arg	His	Cys	Phe	Pro 70	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val 80	
Gly	Ala	Ser	Gly	Asp 85	His	Asp	Asp	Ser	Ala 90	Met	Lys	Thr	Leu	Arg	Asn	٠.
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		Ser. 115					120					125			-	
	130	Pro				135					140		-			
145		Ala			150					155					160	·
		Asp		165					170				_	175		
		Leu	180	-	,			185					190	•		
		<b>A</b> rg 195					200					205		_		
	210	Ile				215					220					
225		Glu			230					235			_	_	240	
		Leu		245					250					255	-	
•	-	Leu	260	٠	-			265					270		-	
		Pro 275					280				· .	285	•			
	290	Leu				295					300		_	_	-	
305		Thr			310					315					320	
		Leu		325					330					335		
		Gln	340					345	•				350		*	
		Gln 355		٠.			360					365		_		٠.
•	370	Glu				375					380		•			
385				-	390					395		•			Lys 400	
		Gln		405					410		•	•		415		
		Met	420		•			425			•	•	430			
		Asn 435					440					445				
	450	Lys				455					460					•
465		Glu			470					475					480	
•		Met		485					490					495	_	
Leu	Lys	Leu	Thr	Ser.	Glu	Glu	Glu	Ser	Gln	Arq	Leu	Glu	Glv	Ser	Glu	

500 505 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys 520 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly 535 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser 550 . 555 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr 565 570 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln 585 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln 600 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys 615 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile 630 635 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu 650

<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

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	Leu		260					265					270		
	Thr	275					280					285			
	Phe 290					295					300				
305					310					315					320
	Ser			325				•	330					335	
	Gly		340					345					350		
	Cys	355				-	360					365		_	
	Ser 370 Glu					375					380				
385					390					395					400
	Ser			405					410					415	Glu
	Glu		420					425	•		*		430		
	Thr	435					440					445			
	Arg 450					455					460				
465	Glu				470					475					480
	Gln			485					490					495	
	Lys		500					505					510		
	Gly	515					520					525		·	
	<b>Asp</b> 530					535					540				
His 545	Gly	Ser	Thr	His	Val 550	Gly	Phe	Pro:	Glu	<b>A</b> sn 555	Leu	Thr	Asn	Gly	
	Ala	Gly	Asn	Gly 565		Asp	Gly	Leu	Ile 570	Pro	Pro	Arg	Lys	Ser 575	560 Arg
Thr	Pro	Glu	Ser 580	Gln	Gln	Phe	Pro	Asp 585	Thr	Glu	Asn	Glu	Glu 590	Tyr	His
	Asp	595			•		600	Lys	Gln	Phe	Cys	605	Glu		
Thr	Gly 610	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His		Glu	Lys	Gln	Ile
Glu	Val	Val	Glu	Lvs	Met	615 Asn	Ser	Glu	Len	Ser	620	Ser	Cyro	I.s.a	Taro
625			•		630					635					640
	Lys			645					650					655	Ala
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<211> 3279
<212> DNA
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cactgggagg ggacateetg cagaaggtag gagtgageaa acaceegetg caggggaggg 180
gagagecetg eggeacetgg gggageagag ggageageac etgeceagge etgggaggag 240
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cagggcgcga gatggcctca cacagggaag agagggcccc teetgcaggg cetcacetgg 360
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aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
gtggctccag gccttgcccc tgcctgggcc ctcacccagc ctccctcaca gtctcctggc 600
ceteagtete teccetecae tecatectee atetggeete agtgggteat tetgateact 660
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cattletgic tgtteetgag agetgggaat tgeteteagt catetgeetg egeggttetg 1020
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gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
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tagecataga gatteacage ecagageagg aggacgetge acaccatgea ggatgacatg 2940
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acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
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gttttcagac cttaaaaaaa aaaaaaaaa aaaagtttt
                                                                  3279
<210> 383
<211> 155
<212> PRT
<213> Homo sapiens
<400> 383
Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
                             10
Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
           20
                                                     30
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
                         55
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
                     70
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
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105

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn

120

135

Ala Leu Glu Arg Gly His Leu Val Arg Glu

110

140

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145

100

115

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<213> Homo sapiens
<400> 384
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ggggaagggt cecttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tececaagae acateetaaa aggtgttgta atggtgaaaa egtetteett etttattgee 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tctttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaa aaaaaaa
                                                                   557
<210> 385
<211> 337
<212> DNA
<213> Homo sapiens
<400> 385
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gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
teteaaagee atetgetgte ttegagtacg gacacateat cacteetgea ttgttgatea 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtocagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattocccc ttttccacat cccggca
<210> 386
<211> 300
<212> DNA
<213> Homo sapiens
<400> 386
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gcgaccttgg eccgaagget ctagcaagga cccaecgacc ccagecgcgg cggcggcggc 180
gcggactttg cccggtgtgt ggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttageet tegetgeeag gaeegtggae egateceagg getgtggtgt aaceteagee 300
<210> 387
<211> 537
<212> DNA
<213> Homo sapiens
<400> 387
gggccgagtc gggcaccaag ggactctttg caggcttect tecteggatc atcaaggetg 60
occepted typeatraty atcageacet atgagttegg caaaagette ttecagagge 120
tgaaccagga eeggettetg ggeggetgaa aggggcaagg aggcaaggac eeegtetete 180
ccacggatgg ggagaggca ggaggagacc cagccaagtg cctttcctc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
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```
geggeecage acttecteag acacaactte tteetgetge teeagtegtg gggateatea 360
cttacccacc ccccaagttc aagaccaaat cttccagctg ccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaaa
<210> 388
<211> 520
<212> DNA
<213> Homo sapiens
<400> 388
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tgaggttaaa ccagtttgca ttcccctaat gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
ggaccccctc cccaacatgc cccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatggtta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tggtgggttt tttttctggt
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens
<400> 389
cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctccccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagectatgg ccagetgtet ttgtgtteec teteaceege etgteeteac agetgagaet 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag
                                                                   365
<210> 390
<211> 221
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G
<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
getetangag tetganenga ntegttgeee canthtgaca naaggaaagg eggagettat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
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```
<220>
<221> misc_feature
<222> (1) ... (325)
<223> n = A, T, C \text{ or } G
<400> 391
tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantingat niccanagee clacecaten tagticiget eleccacegg niaecagee 240
cactgoccag gaatoctaca gocagtacco tgtoccgacg tototaccta ccagtacgat 300
gagaceteeg getactacta tgace
<210> 392
<211> 277
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(277)
<223> n = A,T,C or G
<400> 392
atatigitta acteetteet tiatatetti taacattite atggngaaag giteacatet 60
agteteactt nggenagngn etectaettg agtetettee eeggeetgnn ceagtngnaa 120
antaccanga accgncatgn cttaanaacn neetggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccetgtee actaegrgat getgtaggat taaagtetea cagtgggegg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa
                                                                    277
<210> 393
<211> 566
<212> DNA
<213> Homo sapiens
<400> 393
actagiccag igiggiggaa ticgeggeeg egiegaegga caggicagei gietggetea 60
gtgatetaea ttetgaagtt gtetgaaaat gtetteatga ttaaatteag eetaaaegtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatatca ggactggtta cttggttaag 240
gaggggtcta ggagatetgt ecettttaga gacaeettae ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgteetgt atteegatga teateetgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaa 480
cattetetge etgagtttta attttgtee aaagttattt taatetatae aattaaaage 540
ttttgcctat caaaaaaaa aaaaaa
                                                                   566
<210> 394
<211> 384
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
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<222> (1)...(384)
<223> n = A,T,C or G
<400> 394
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
teccaagatt ategggagaa agggggeagt aattacecaa ateeggttgg agcatgaegt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt
<210> 395
<211> 399
<212> DNA
<213> Homo sapiens
<400> 395
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttetet ttggaaagee tgggeatete eteactacag acetetgace atgggaeggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac
<210> 396
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(403)
<223> n = A,T,C or G
<400> 396
tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt
<210> 397
<211> 100
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(100)
<223> n = A,T,C or G
```

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actagincag tgiggiggaa ticgeggeeg egiegaeeta naaneeatei etatageaaa 60
tccatccccg ctcctggttg gtnacagaat gactgacaaa
<210> 398
<211> 278
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(278)
\langle 223 \rangle n = A,T,C or G
<400> 398
geggeegegt egacageagt teegeeageg etegeeeetg ggtggggatg tgetgeaege 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agcccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg
                                                                    278
<210> 399
<211> 298
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G
<400> 399
acggaggtgg aggaagcgnc cctgggatcg anaggatggg toctgncatt gaccncctcn 60
ggggtgeeng catggagege atgggegegg geetgggeea eggeatggat egegtggget 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg
<210> 400
<211> 548
<212> DNA
<213> Homo sapiens
<400> 400
acatcaacta cttectcatt ttaaggtatg gcagtteett teatecett tteetgeett 60
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
caaagaacca cacgettaga agggtaagag ggcaccctat gaaatgaaat ggtgatttet 180
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatoccg 300
tataccetet caecatecce ttgtctacte tgatgccccc aagatgcaac tgggcageta 360
gttggcccca taattctggg cetttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggccccc ctcctgggat caagcccctc ccaggecetg 480
tecceagece etectgeece ageceaeceg ettgeettgg tgetcagece teccattggg 540
agcaggtt
```

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<210> 401
<211> 355
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (355)
<223> n = A,T,C or G
<400> 401
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggt ggcctatttc agctgctftg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(407)
<223> n = A,T,C or G
<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggaget teteceetge agagagteee tgateteeca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa
                                                                   407
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (303)
<223> n = A, T, C or G
<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcaccaaa 60
tectaageaa gageeatgge atggtgaaaa tgeaaaagga gagtetggee aatetacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
```

```
<210> 404
<211> 225
<212> DNA
<213> Homo sapiens
<400> 404
aagtgtaact tttaaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacaq 120
acattttcca ctcgtgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat
<210> 405
<211> 334
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (334)
<223> n = A,T,C or G
<400> 4.05
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac etecececat agtgaateag ettecagggg gtecagtece teteettact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctqtqaqtqt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatqt 300
cactetecac teteteanng tggateceac cect
<210> 406
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(216)
<223> n = A,T,C or G
<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
achaaacaca aattinatgi tgcacccitg titctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant
                                                                   216
<210> 407
<211> 413
<212> DNA
<213> Homo sapiens
<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg-caaatggatg tcatgcacgt accttcattt 240
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```
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag
<210> 408
<211>.183
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (183)
<223> n = A,T,C or G
<400> 408
ggagetngee eteaatteet eeatntetat gttaneatat ttaatgtett ttgnnattaa 60
tncttaacta gttaatcctt aaagggctan ntaatcctta actagtccct ccattgtgag 120
cattatectt ccagtatten cettetnttt tatttactcc tteetggeta eccatgtact 180
ntt
<210> 409
<211> 250
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (250)
<223> n = A, T, C or G
<400> 409
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct coccttcttt ctgctcacgg ccttatctag 180
getteecagt geceecagga cagegtggge tatgtttaca gegenteett getggggggg 240
ggccntatgc
                                                                   250
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (306)
<223> n = A,T,C or G
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtettgeaa teccatttge aggateegte tgtgeacatg cetetgtaga gageageatt 120
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atcttttta aactggaaag ttcaattgng aaaatgaata 300
tentge
                                                                   306
```

```
<210> 411
<211> 261
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(261)
\langle 223 \rangle n = A,T,C or G
<400>.411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggngaggcaa a
<210> 412
<211> 241
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(241)
<223> n = A,T,C or G
<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agectgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
<210> 413
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (231)
<223> n = A,T,C or G
<400> 413
aactettaca atecaagtga eteatetgtg tgettgaate etttecaetg teteatetee 60
ctcatccaag tttctagtac cttctcttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc teetcatttg gaacetaaaa actetettet teetgggtet gagggeteea 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t
                                                                    231
<210> 414
<211> 234
<212> DNA
<213> Homo sapiens
```

```
<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagetg aaaacataac ccactetgte etggaggeac tgggaageet agagaagget 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca
<210> 415
 <211> 217
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A,T,C or G
<400> 415
gcataggatt aagactgagt atcttttcta cattcttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc
                                                                    217
<210> 416
<211> 213
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C \text{ or } G
<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag
                                                                    213
<210> 417
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
\langle 223 \rangle n = A,T,C or G
<400> 417
nagtetteag geceateagg gaagtteaca etggagagaa gteatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt
```

```
<210> 418
<211> 328
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G
<400> 418
tttttggcgg tggtggggca gggacgggac angagtetea etetgttgee caggetggag 60
tgcacaggca tgatctcggc tcactacaac coctgoctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactootga ootcaagtga totgoocaco tcagootcoc 300
aaagtgctan gattacaggc cgtgagcc
<210> 419
<211> 389
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A, T, C or G
<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
acceptgage catggactgg agectgaaag geagegtaca ecetgeteet gatettgetg 120
cttgttteet etetgtgget ceatteatag cacagttgtt geactgagge ttgtgcagge 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
ceggttetee agecaceaac etcacteget ecegeaaatg geacateagt tettetacee 300
taaaggragg accaaagggc atetgetttt etgaagteet etgetetate agccateaeg 360
tggcagccac tcnggctgtg tcgacgcgg
<210> 420
<211>.408
<212> DNA
<213> Homo sapiens
<400> 420
gtteeteeta aeteetgeea gaaacagete teeteaacat gagaqetgea coecteetee 60
tggccagggc agcaagectt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agecaaggag ttgaagtttg tgactttggt gttteggeat ggagacegaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaqqatttq 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaagcacag 360
acgttgaccg gactttgatg aagtgctatg acaaacctgg caagcocg
<210> 421
<211> 352
<212> DNA
```

```
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(352)
<223> n = A,T,C or G
<400> 421
gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cacteegagt ttattgggtg tttgtttcct ttgagateca tgcatttcct gg
<210> 422
<211> 337
<212> DNA
<213> Homo sapiens
<400> 422
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcgg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(310)
<223> n = A, T, C or G
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tractgarag aaraggeett tetteggere tettetera cracgatata ettgragter 180
teettettga agattetttg geagttgtet ttgteataae eeacaggtgt anaaacaagg 240
gtgcaacatg aaatttetgt ttegtageaa gtgcatgtet cacagttgte aagtetgeec 300
tccgagttta
<210> 424
<211> 370
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(370)
\langle 223 \rangle n = A,T,C or G
```

```
<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtettt tttgggteet tetteteeac cacgatatac ttgcagteet 180
ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg
                                                                370
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G
<400> 425
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattateca ttatnttaag ggttgaette aggntacage acacagaeaa acatgeecag 180
gaggntntca ggaccgctcg atgtnttntg aggagg
<210> 426
<211> 596
<212> DNA
<213> Homo sapiens
<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg octtcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg teccatecca ggacettoca teggegagta cetgggagee egtget
<210> 427
<211> 107
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G
<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggneccag 60
```

```
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng
                                                                   107
<210> 428
<211> 38
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G
<400> 428
gaacttccna anaangactt tattcactat tttacatt
                                                                   38
<210> 429
<211> 544
<212> DNA
<213> Homo sapiens
<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actettgaag gactttetga tttatccaca atcaaatcat eggtttteag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
geetteeact teagttacae eteacteace atecteteet gttggttetg tgetgettea 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat
<210> 430
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(507)
<223> n = A,T,C or G
<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattetecte tggcetetaa tagteaatga ttgtgtagee atgeetatea gtaaaaagat 480
ttttgagcaa aaaaaaaaa aaaaaaa
<210> 431
```

<211> 392

```
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (392)
<223> n = A,T,C or G
<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaqa 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
                                                                    392
<210> 432
<211> 387
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (387)
<223> n = A,T,C or G
<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tottattctt ttgtctataa tactgtattg 120
ngtagtecaa geteteggna gtecagecae tgngaaacat geteeettta gattaacete 180
gtggacnetn tigitgnatt gtetgaactg tagngeeetg tattitgett etgtetgnga 240
attetgttgc ttetggggca ttteettgng atgeagagga ecaecacaca gatgacagca 300
atctgaattg ntecaatcac agetgegatt aagacatact gaaategtac aggaceggga 360
acaacgtata gaacactgga gtccttt
<210> 433
<211> 281
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G
<400> 433
ttcaactage anagaanact getteagggn gtgtaaaatg aaaggettee acgeagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggenetat ttgggttgge tggaggget gtggaaaaca tggagagatt ggegetggag 180
ategeegtgg ctatteeten ttgntattae accagngagg ntetetgtnt geecactggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t
<210> 434
<211> 484
```

```
<212> DNA
<213> Homo sapiens
<400> 434
ttttaaaata agcatttagt gctcagtccc tactgagtac tctttctctc ccctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagectgttt ctatectgtt taataaatta gtttgggtte tetacatgea taacaaacce 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta
<210> 435
<211> 424
<212> DNA
<213> Homo sapiens
<400> 435
gegeegetea gageaggtea etttetgeet tecaegteet eetteaagga ageeecatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aacccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggagggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggcct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
<210> 436
<211> 667
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(667)
<223> n = A,T,C or G
<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tectggecat gtaateetga aagtttteee aaggtageta taaaateett ataagggtge 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagtteetga aaggeaggta tageaactga tetteagaaa gaggaactgt gtgeaceggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gecaggiting teatageact cateaaagte eggicaaegt etgigetieg aatataaaec 360
tgttcatgtt tataggactc attcaagaat tttctatatc tcttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gatteettta tggggteagt gggaaaggtg teaatgggae tteggtetee atgeegaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag
                                                                  667
<210> 437
<211> 693
```

```
<212> DNA
<213> Homo sapiens
<400> 437
ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttqt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
aggtactect etatttteac ecetettget tetactetet ggeagteaga ectgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
cattteteca ggttacceta ggtgtcacta ttggggggac agccagcate tttagettte 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tectatttet aggeactgag ggetgtgggg tacettgtgg tgecaaaaca gateetgtt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc
                                                                 693
<210> 438
<211> 360
<212> DNA
<213> Homo sapiens
<400> 438
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggtgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
geetetaata gteaataatt gtgtageeat geetateagt aaaaagattt ttgageaaac 360
<210> 439
<211> 431
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A, T, C or G
<400> 439
gtteetnnta actectgeea gaaacagete teeteaacat gagagetgea eccetectee 60
tggccagggc agcaagcett ageettgget tettgtttet getttttte tggctagace 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaocgaa 180
gtcccattga cacctttecc actgacceca taaaggaatc ctcatggeca caaggatttq 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attottgaat gagtootata aacatgaaca ggtttatatt ogaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t
                                                                431
<210> 440
<211> 523
<212> DNA
<213> Homo sapiens
```

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<400> 440
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctetttg tgteeettgg teetggaaca tttatgttee ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta
<210> 441
<211> 430
<212> DNA
<213> Homo sapiens
<400> 441
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaageacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag
<210> 442
<211> 362
<212> DNA
<213> Homo sapiens
<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtggggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc
<210> 443
<211> 624
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G
<400> 443
ttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggagggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgettatt ttaaaagaaa tgtaaagage agaaageaat teaggetace etgeettttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
```

```
eccaaaceae agaaaatggg grgaaattgg ccaactttet attaacttgg ettectgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca teettattat taaagteaac getaaaatga atgtgtgtge atatgetaat 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgettgt getgggteea aatettggte tactatgace ttggeeaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(425)
<223> n = A,T,C or G
<400> 444
gcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagettigt ccaggeeigt gigigaacee aatgittige tiagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
octotgoaat otgocaccto otgotggoag gatttgtttt tgcatcotgt gaagagcoaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga
                                                                   425
<210> 445
<211> 414
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G
<400> 445
catgittatg nittiggatt actitigggca octagigtti ctaaatcgic tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattett tgeatgtgge agattattgg atgtagttte etttaactag catataaate 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag
<210> 446
<211> 631
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ...(631)
```

 $\langle 223 \rangle$  n = A,T,C or G

```
<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg teeggaacat tacaatggct 60
tetgeatgea tgggaagtgt gageatteta teaatatgea ggageeatet tgeaggtgtg 120
atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g
<210> 447
<211> 585
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G
<400> 447
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attectttat ggggtcagtg ggaaaggtgt caatgggact teggteteca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta
                                                                   585
<210> 448
<211> 93
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(93)
<223> n = A,T,C or G
<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag
<210> 449
<211> 706
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(706)
<223> n = A, T, C or G
<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtggqtca 60
ttctgancac cgaactgacc atgocagecc tgccgatggt cctccatggc tccctaqtqc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
eggggacage atcetgcaga tggtegggeg egteceatte gecatteagg etgegcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatect ctagagegge egectactae tactaaatte geggeeget 480
cgacgtggga tecncactga gagagtggag agtgacatgt getggaenet gtecatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcnccca 660
706
<210> 450
<211> 493
<212> DNA
<213> Homo sapiens
<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatateet atagtggaaa taagagagte 120
aaatgagget gagaacttta caaagggate ttacagacat gtegecaata teactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggracaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg teagagagtt aaaaagtgag ttetateeat gaggtgatte cacagtette 360
tcaagtcaac acatctgtga actcacagac caagttetta aaccactgtt caaactetge 420
tacacatcag aatcacctgg agagetttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag
<210> 451
<211> 501
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) . . . (501)
<223> n = A,T,C or G
<400> 451
gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaattagg 180
tgacnetata gaagagetat gacgtegeat geacgegtae gtaagettgg atectetaga 240
geggeegeet actactacta aattegegge egegtegaeg tgggateene actgagagag 300
tggagagtga catgtgctgg acnotgreea tgaagcactg agcagaaget ggaggcacaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactoca 480
```

```
tcttaaaaaa aaaaaaaaa a
                                                                   501
<210> 452
<211> 51
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A, T, C or G
<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c
<210> 453
<211> 317
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G
<400> 453
tacatettge ttttteecca ttggaactag teattaacce atetetgaac tggtagaaaa 60
acatetgaag agetagteta teageatetg geaagtgaat tggatggtte teagaaceat 120
ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc tttatta
<210> 454
<211> 231
<212> DNA
<213> Homo sapiens
<400> 454
ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attettetge atcccagett gcaaacaaaa ttgttettet aggtetecae 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t
<210> 455
<211> 231
<212> DNA
<213> Homo sapiens
<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggctcc tttctcctct a
```

```
<210> 456
<211> 231
<212> DNA
<213> Homo sapiens
<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcgtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120
tgcactcaaa ttoctttato aggaataact acatagocac tatttacaaa gocattggaa 180
cetttttatt tggtgeaget getagteagt ceetgactga cattgecaag t
<210> 457
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G
<400> 457
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agaccettga gatcattaag etttqtatee 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g
<210> 458
<211> 231
<212> DNA
<213> Homo sapiens
<400> 458
aggiciggit coccecacit coactoccct ctactototo taggaciggg ctgggccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t
<210> 459
<211> 231
<212> DNA
<213> Homo sapiens
<400> 459
ggtaccgagg ctcgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
gecetgeact gittiecete caecacagee atectgiece teatiggete igigettiec 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a
<210> 460
<211> 231
<212> DNA
<213> Homo sapiens
<400> 460
```

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gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagettg gtecageete cagtecacee etaccagget taaggataga a
<210> 461
<211> 231
<212> DNA
<213> Homo sapiens
<400> 461
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcctg tgtgtcctgg 120
gtggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t
<210> 462
<211> 231
<212> DNA
<213> Homo sapiens
<400> 462
aggtaccete attgtageea tgggaaaatt gatgtteagt ggggateagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a
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<211> 231
<212> DNA
<213> Homo sapiens
<400> 463
actgagtaga caggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180
tggggaggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c
<210> 464
<211> 231
<212> DNA
<213> Homo sapiens
<400> 464
gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgact 60
aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120
cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c
<210> 465
<211> 231
<212> DNA
<213> Homo sapiens
<400> 465
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catgitgitg tagctgiggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60
gtggcaaatt agcaacaaat tctgacatca tatttatggt ttctgtatct ttgttgatga 120
aggatggcac aattitigct tgtgttcata atatactcag attagttcag ctccatcaga 180
taaactggag acatgcagga cattagggta gtgttgtagc tctggtaatg a
<210> 466
<211> 231
<212> DNA
<213> Homo sapiens
<400> 466
caggiacete titecatigg atacigiget ageaageatg cicleogggg tittitaat 60
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaacat ttgcccagga 120
cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180
aataatggag accagtccca caagatgaca accagtcgtt gtgtgcggct g
<210> 467
<211> 311
<212> DNA
<213> Homo sapiens
<400> 467
gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60
tggrggcttt teteettttt cateaagaet ceteageagg gageecagae cageetgeae 120
tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagrga ctgtcatgtg 180
gcatgggtct ctgcccaage tegtaatgag actatageaa ggeggetgtg ggaegteagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c
                                                                 311
<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens
<400> 468
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aagatetgea tggtgggaag gacetgatga tacagagttt gataggagae aattaaagge 120
tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtggttcaa 240
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gtgaatgtgg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360
aaatgggata cacagtatga tetataaagt gggatatagt atgatetaet teactgggtt 420
atttgaagga tgaattgaga taatttattt caggtgeeta gaacaatgee cagattagta 480
cattleggegg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540
gattatcatt caatctcata gttttgtcat ggoccaattt atoctcactt gtgoctcaac 600
aaattgaact gttaacaaag gaatctctgg teetgggtaa tggctgagca ecactgagca 660
tttecattee agttggette ttgggtttge tagetgeate actagteate ttaaataaat 720
gattaaataa agaacttgag aagaacaggt ttcattaaac ataaaatcaa tgtagacgca 840
aattttctgg atgggcaata cttatgttca caggaaatgc tttaaaatat gcagaagata 900
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ggatgtteet tagteactta aaggagaact gaaaaatage agtgagttee acataateea 1020
acctgtgaga ttaaggctct ttgtggggaa ggacaaagat ctgtaaattt acagtttcct 1080
tecaaageca acgtegaatt ttgaaacata teaaagetet tetteaagae aaataateta 1140
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```
tttagctctc aaaatggttc attttaagag aaagttttag aatctcatat ttattcctgt 1260
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atgcaacaaa caaaatggaa tactgtgatg acatgaggca gccaagctgg ggaggagata 1800.
accacggggc agagggtcag gattctggcc ctgctgccta aactgtgcgt tcataaccaa 1860
atcatttcat atttctaacc ctcaaaacaa agctgttgta atatctgatc tctacggttc 1920
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## **PCT**

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### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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A61K 39/395, G01N 33/68, 33/574, C07K
16/30, C12N 15/62, 5/02 // A61P 35/00

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(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,

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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

#### (57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific f r cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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Internet and Application No PCT/US 99/15838

CLASSIFICATION OF SUBJECT MATTER PC 7 C12N15/12 C07K14/47 A61K39/395 G01N33/68 C12Q1/68 G01N33/574 C12N5/02 C07K16/30 C12N15/62 //A61P35/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. 1-22. WO 97 33909 A (CORIXA CORP) 29-31. 18 September 1997 (1997-09-18) 35-49. 53-79 the whole document 23-28. SJOGREN H O: "Therapeutic immunization 32-34. against cancer antigens using genetically 53-57 engineered cells" IMMUNOTECHNOLOGY, vol. 3, no. 3, 1 October 1997 (1997-10-01), pages 161-172, XP004097000 ISSN: 1380-2933 the whole document Patent family members are listed in annex. Further documents are listed in the continuation of box C. X Special categories of cited documents : "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-\*O" document referring to an oral disolosure, use, exhibition or ments, such combination being obvious to a person skilled in the crt. document published prior to the international filing date but later than the priority date claimed \*&\* document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search **1** 4. 85. 00 31 January 2000 Authorized officer

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Fax: (+31-70) 340-3016

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

ANDRES S.M.

International Application No PC7, US 99/15838

		1,72 33/12020
C.(Continua Category *.	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHU R S ET AL: "CPG OLIGODEOXYNUCLEOTIDES ACT AS ADJUVANTS THAT SWITCH ON T HELPER 1 (TH1) IMMUNITY" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 186, no. 10,	14-20, 25-27, 41-47
• •	1 November 1997 (1997-11-01), pages 1623-1631, XP002910130 ISSN: 0022-1007 the whole document	
A	EP 0 317 141 A (BECTON DICKINSON CO) 24 May 1989 (1989-05-24) the whole document	50-52
A	ZITVOGEL L ET AL: "Eradication of established murine tumors using a novel cell-free vaccine: dendritic cell-derived exosomes" NATURE MEDICINE,	
٠.	vol. 4, no. 5, 1 May 1998 (1998-05-01), pages 594-600, XP002085387 ISSN: 1078-8956 cited in the application	
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		34,35, 39-42, 44-46, 48,49, 58-79
	page 3, line 20 -page 22, line 2 page 35, line 9 - last line page 76, line 34 -page 78, line 22 claims	36-79
P,X	WO 98 37418 A (CORIXA CORP) 27 August 1998 (1998-08-27)	1-15, 17-19, 21,22,
	to any any analytic ex	29-31, 34,35, 39-42,
		44-46, 48,49, 58-79
	page 2 -page 24 example 2 page 35, line 15 -page 36, line 11	
	page 81, line 14 -page 83, line 11 claims	
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In ational application No.

PCT/US 99/15838

B x I Ob ervation	ns where certain claim w	ere found unsearchable (C ntinu	ation fit m 1 of first he t)
This International Searc	ch Report has not been establis	shed in respect of certain claim under A	rticle 17(2)(a) for the foll wing reasons:
Remark: /	Although claims 29- are directed to a m	uired to be searched by this Authority, no -34, 48-49, 52, 55-57 method of treatment of t as been carried out and pound/composition.	he human/animal
2. Claims Nos.: because they	relate to parts of the internation	nal Application that do not comply with th arch can be carried out, specifically:	se prescribed requirements to such
	*		
3. Claims Nos.: because they	are dependent claims and are r	not drafted in accordance with the secon	nd and third sentences of Rule 6.4(a).
Box II Observation	ns where unity of invention	n is lacking (Continuation of item	2 of first sheet)
This International Sear	ching Authority found multiple in	nventions in this international application	, as follows:
see additio	*		
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1. As all required searchable dis	l additional search fees were tin aims.	mely paid by the applicant, this Internatio	onal Search Report covers all
2. As all searcha of any addition		vithout effort justifying an additional fee,	this Authority did not invite payment
3. As only some covers only the	of the required additional searc ose claims for which fees were	th fees were timely paid by the applicant paid, specifically claims Nos.:	, this International Search Report
		: \	·
4. X No required as restricted to th	ditional search fees were timel	ly paid by the applicant. Consequently, the claims, it is covered by claims Nos.:	his International Search Report is
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Remark on Protest		The additional search fees were	accompanied by the applicant's protest.
		No protest accompanied the payer	ment of additional search fees.

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### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 1. Claims: 1-79 (all partially)

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

Inventions 2. to 439. Claims: 1-79 (all partially and as far as applicable)

As for subject 1. but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328,330,332-335,340-375,381,382 and 384-472.

mation on patent family members

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